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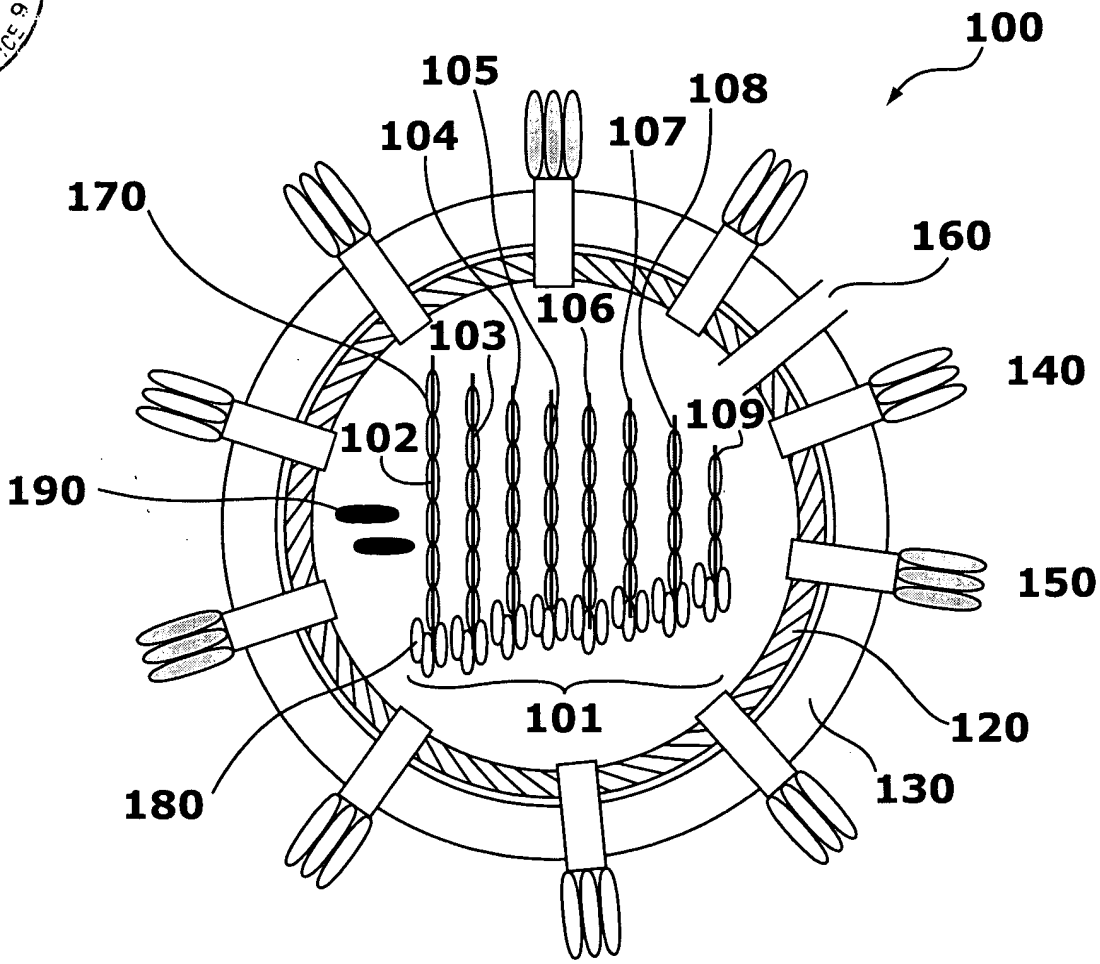

FIG. 1A

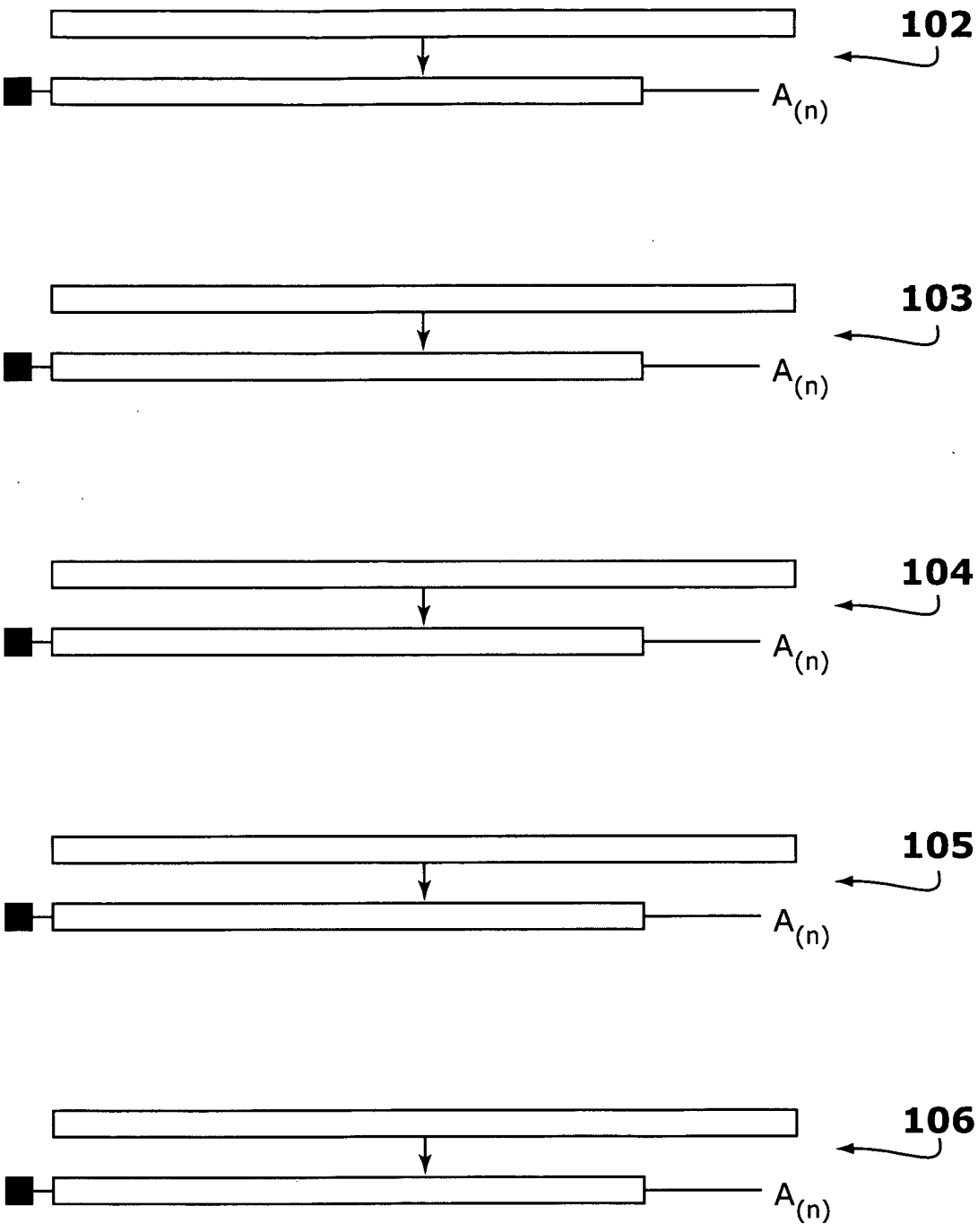

FIG. 1B-1

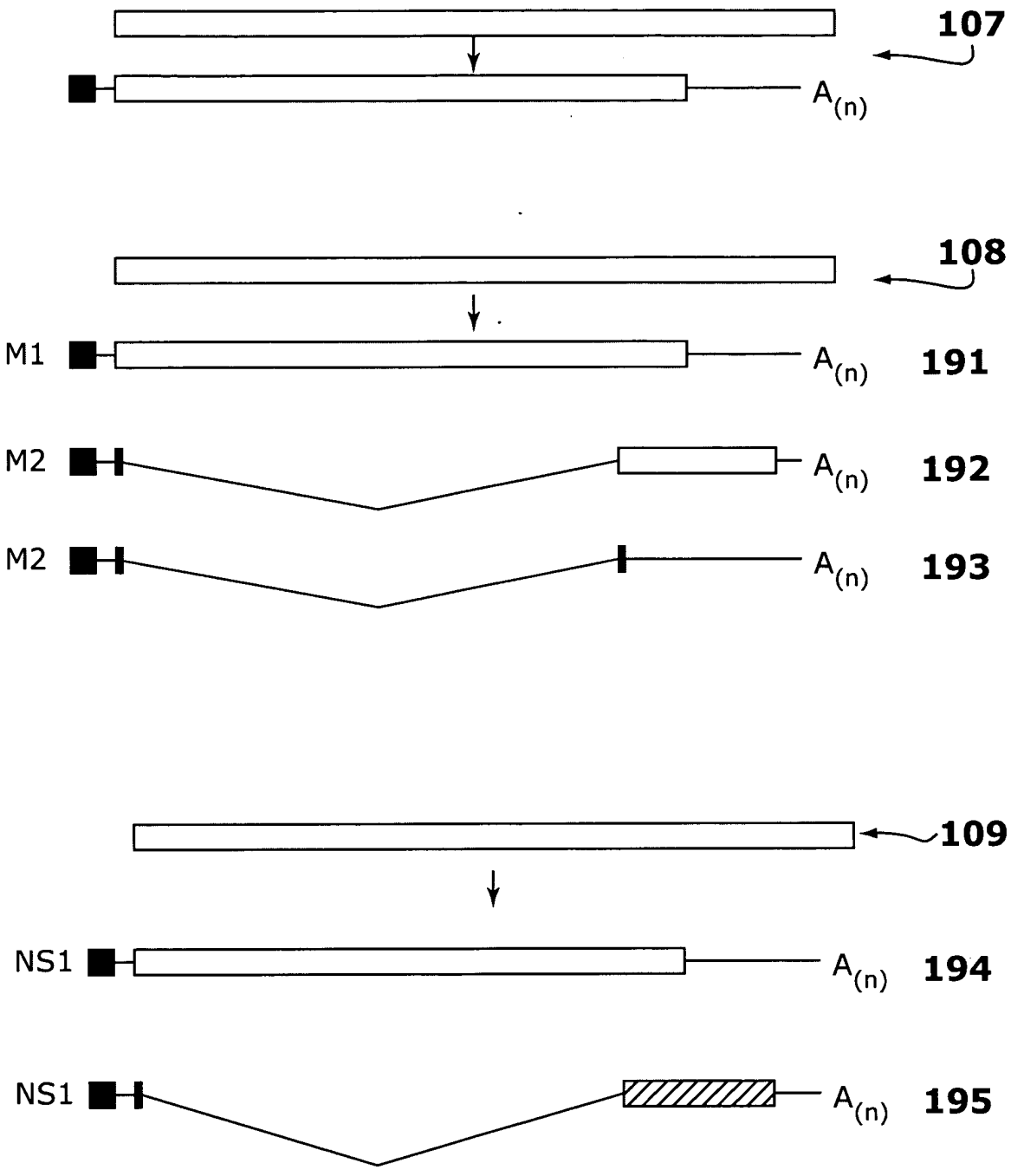

FIG. 1B-2

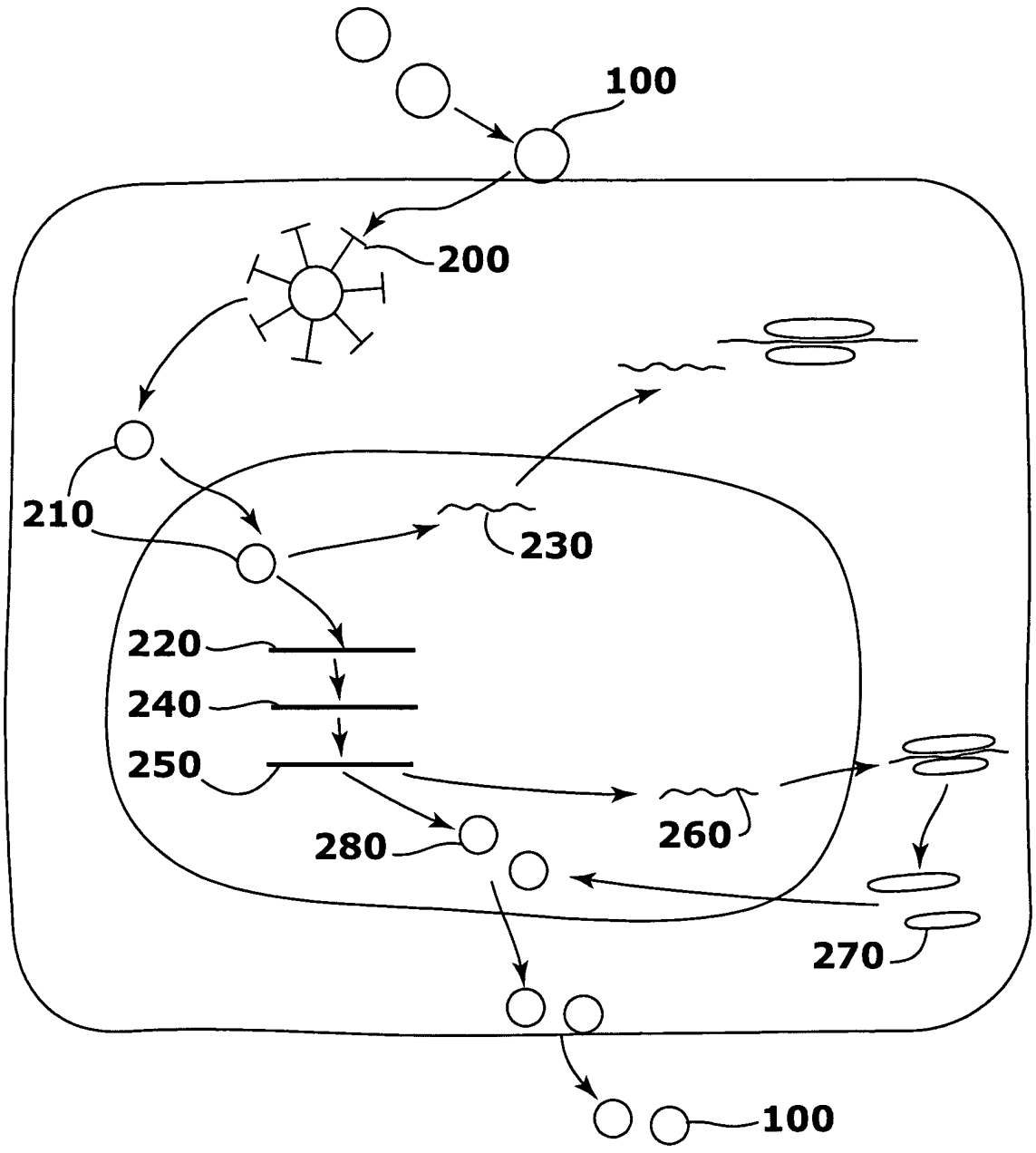

FIG. 2

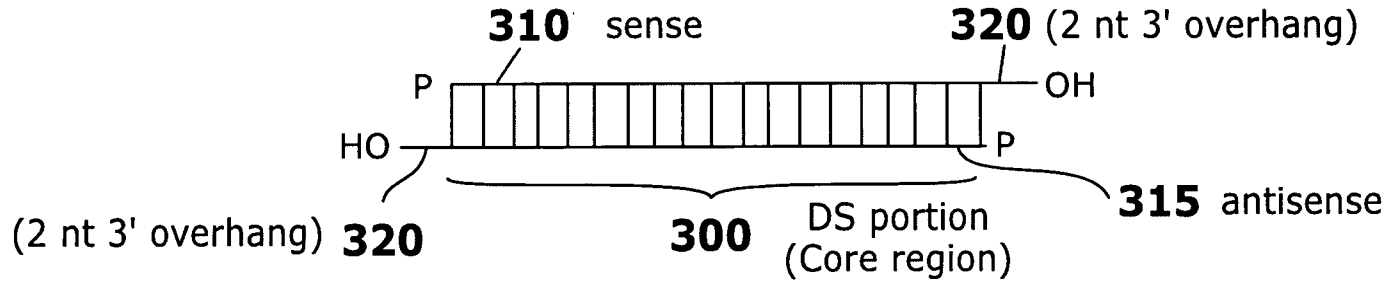
310 sense
320 (2 nt 3' overhang)
P
OH
HO
P
315 antisense
(2 nt 3' overhang) 320
300 DS portion
(Core region)

FIG. 3

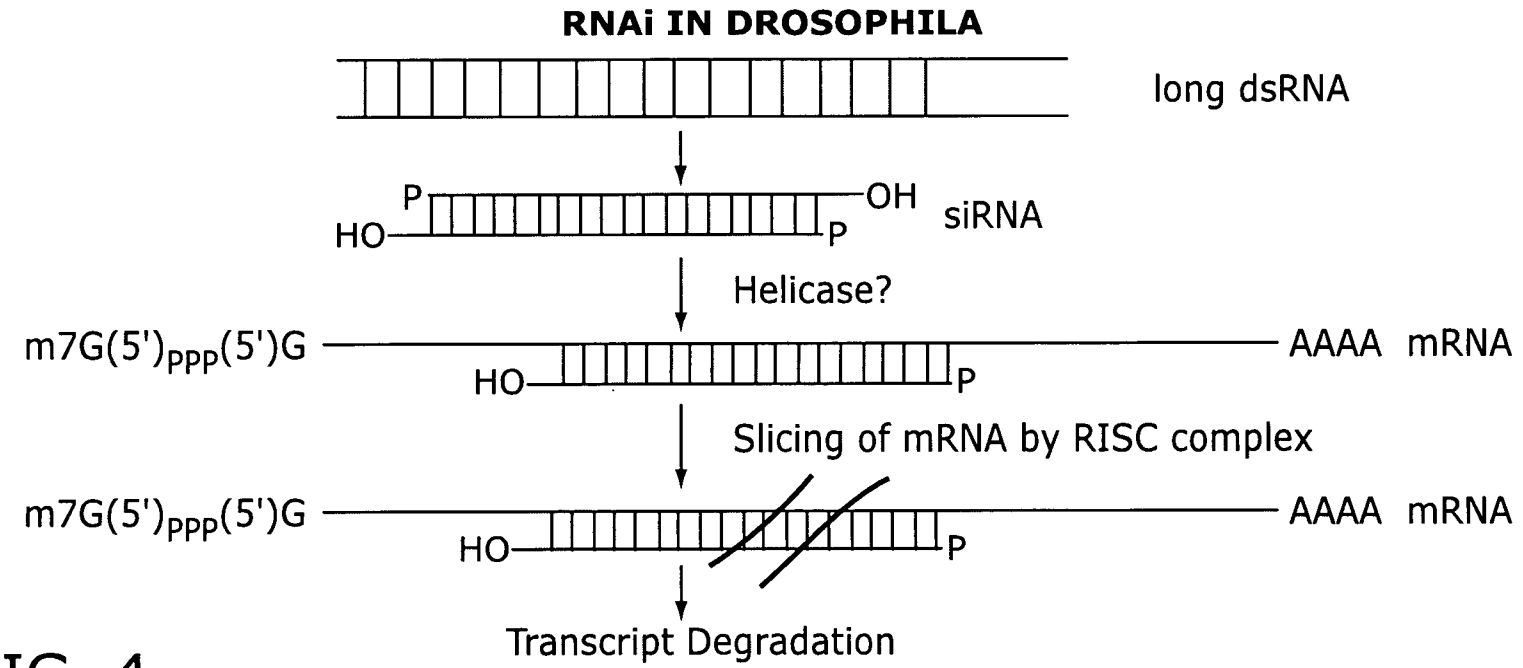
RNAi IN DROSOPHILA
long dsRNA
P
OH
HO
P
siRNA
Helicase?
m7G(5')PPP(5')G
AAAA mRNA
HO
P
Slicing of mRNA by RISC complex
m7G(5')PPP(5')G
AAAA mRNA
HO
P
Transcript Degradation

FIG. 4

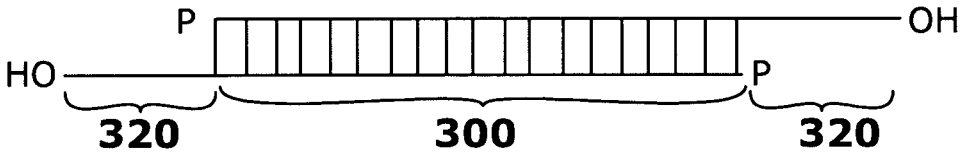

FIG. 5A

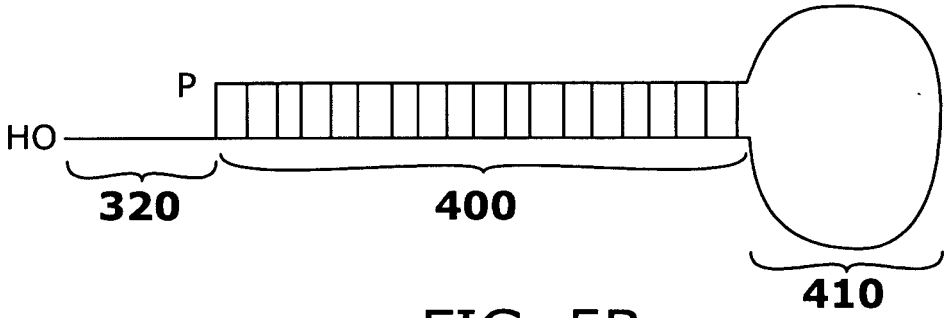

FIG. 5B

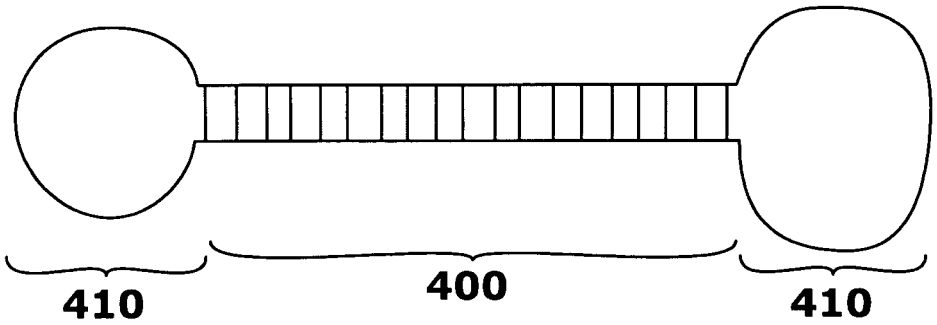

FIG. 5C

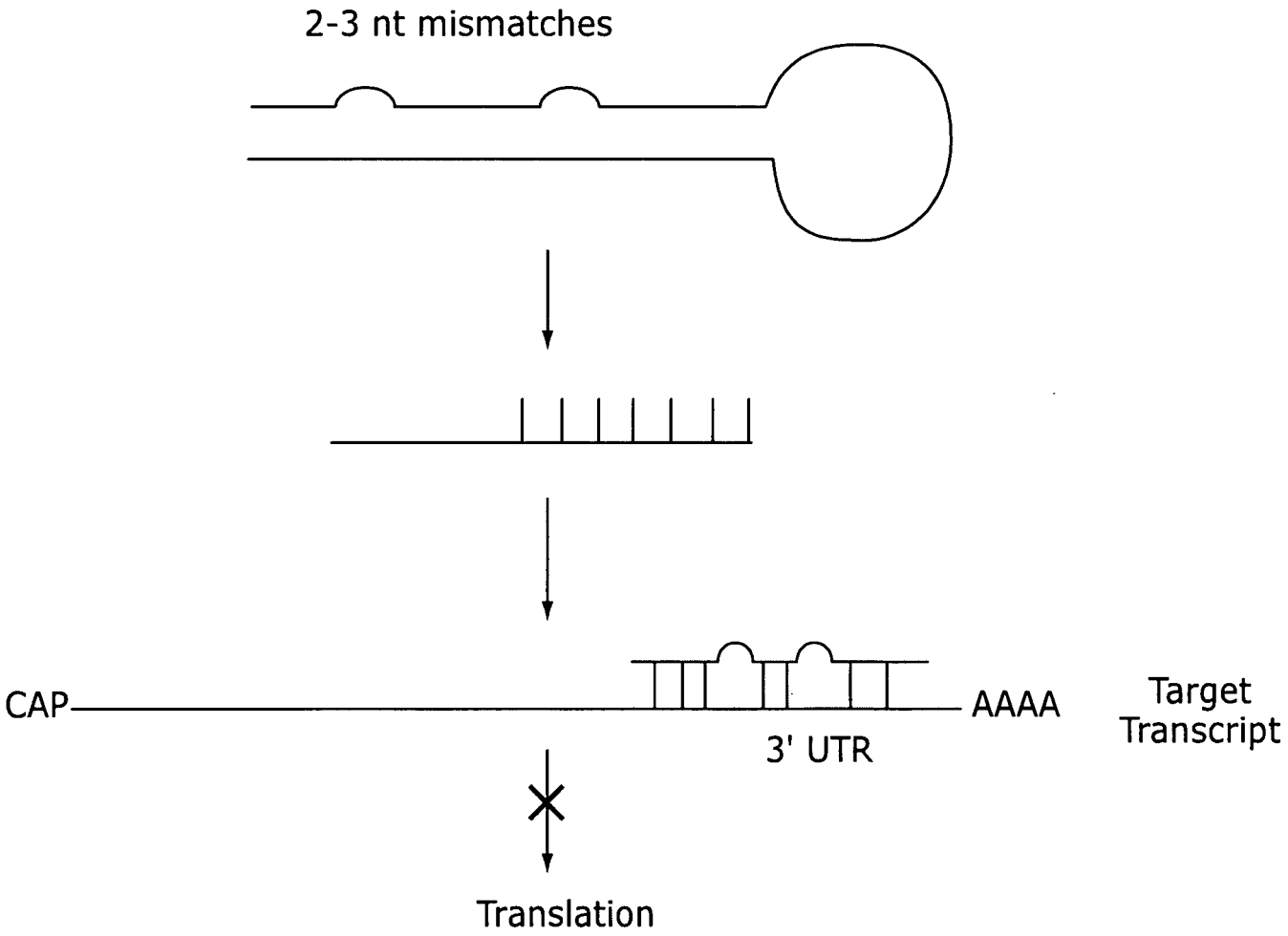
2-3 nt mismatches
CAP
AAAA
3' UTR
Target
Transcript
Translation

FIG. 6

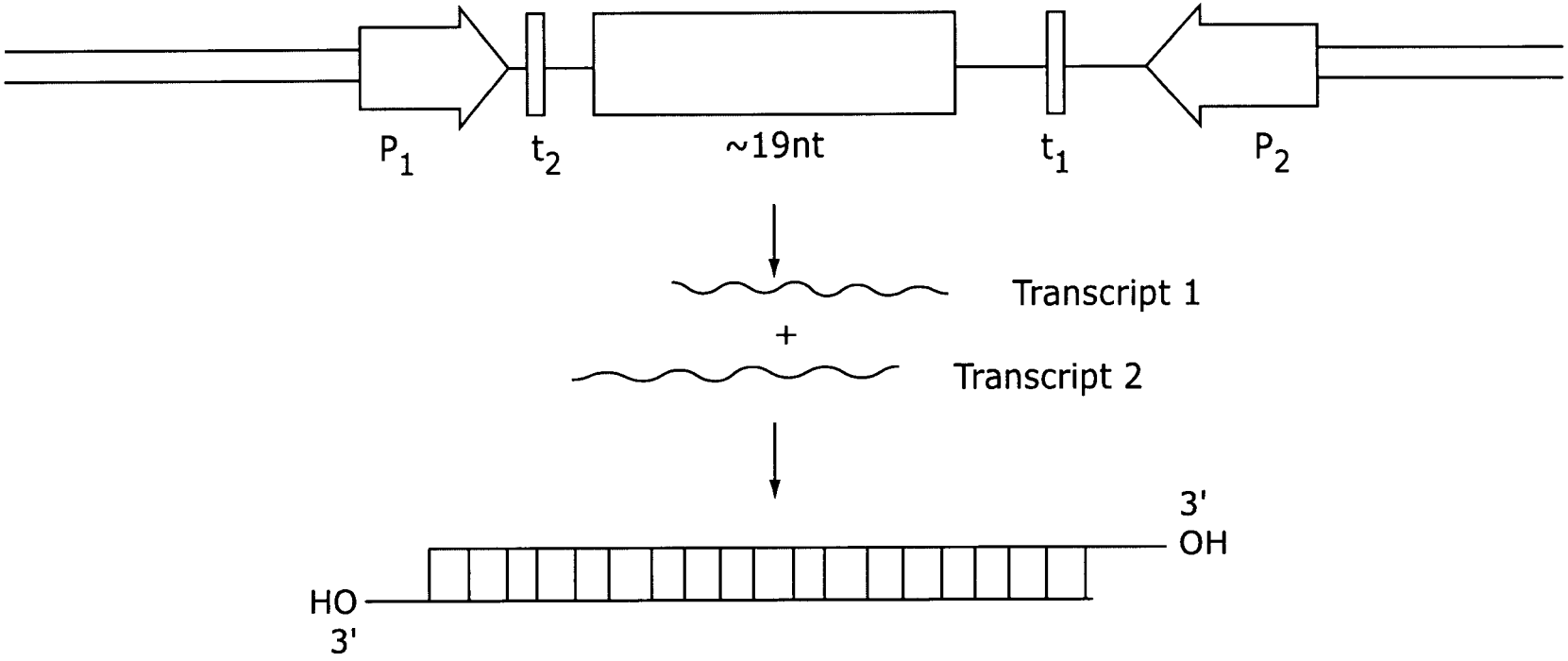

FIG. 7

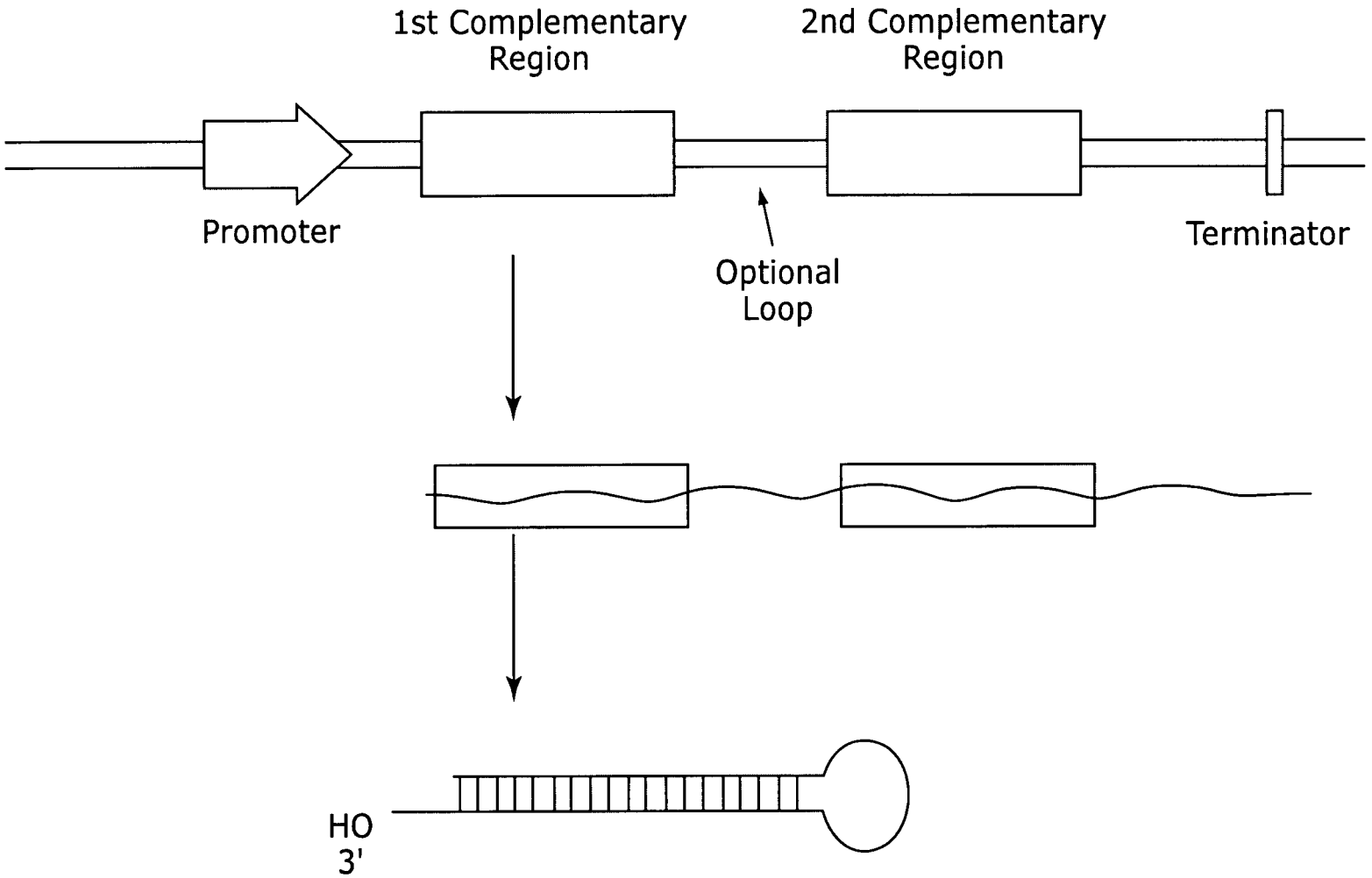
1st Complementary Region
2nd Complementary Region
Promoter
Optional Loop
Terminator
HO
3'

FIG. 8

CLUSTAL W(1.4) multiple sequence alignment

Shaded area: Highly conserved regions selected as siRNA sequences.

Genbank Acc. No.	Strain			Length
NC_002022	A/Puerto Rico/8/34	H1N1	1934	2233 nt
X17336	A/WSN/33	H1N1	1933	2233 nt
M81579	A/Leningrad/134/17/57	H2N2	1957	2233 nt
AF348174	A/Hong Kong/1/68	H3N2	1968	2209 nt
AF257193	A/Hong Kong/481/97	H5N1	1997	2233 nt
AF257191	A/Hong Kong/1073/99	H9N2	1999	2233 nt

```
NC_002022/-      AGCGAAAGCAGGTACTGATCCAAAATGGAAGATTTTGTGCGACAATGCTT
X17336/-         AGCGAAAGCAGGTACTGATTCAAAATGGAAGATTTTGTGCGACAATGCTT
M81579/-         AGCAAAAGCAGGTACTGATCCGAAATGGAAGAATTTGTGCGACAATGCTT
AF348174/-       ----------ATGGAAGATTTTGTACGACAATGCTT
AF257193/-       AGCAAAAGCAGGTACTGATCCAAAATGGAAGACTTTGTGCGACAATGCTT
AF257191/-       AGCAAAAGCAGGTACTGATCCGAAATGGAAGACTTTGTGCGACAATGCTT

NC_002022/-      CAATCCGATGATTGTCGAGCTTGCGGAAAAAACAATGAAAGAGTATGGGG
X17336/-         CAATCCGATGATTGTCGAGCTTGCGGAAAAGGCAATGAAAGAGTATGGAG
M81579/-         CAATCCGATGATTGTCGAGCTTGCTGAAAAAGCAATGAAAGAGTATGGAG
AF348174/-       TAATCCGATGATTGTCGAACTTGCGGAAAAGGCAATGAAAGAGTATGGAG
AF257193/-       CAATCCAATGATTGTCGAGCTTGCGGAAAAGACAATGAAGGAGTATGGGG
AF257191/-       CAATCCAATGATTGTCGAGCTTGCGGAAAAGACAATGAAGGAATATGGGG

NC_002022/-      AGGACCTGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
X17336/-         AGGACCTGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
M81579/-         AGGATCGGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
AF348174/-       AGGATCTTAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
AF257193/-       AAGATCCGAAGATTGAAACAAACAAGTTCGCTGCAATATGCACACACTTA
AF257191/-       AAGACCCGAAAATTGAAACAAATAAGTTCGCTGCAATATGCACACACTTA

NC_002022/-      GAAGTATGCTTCATGTATTCAGATTTCCACTTCATCAATGAGCAAGGCGA
X17336/-         GAAGTGTGCTTCATGTATTCAGATTTTCACTTCATCGATGAGCAAGGCGA
M81579/-         GAAGTATGCTTCATGTATTCAGATTTTCATTTCATCAATGAGCAAGGCGA
AF348174/-       GAAGTATGCTTCATGTATTCAGATTTTCATTTCATCAATGAGCAAGGCGA
AF257193/-       GAAGTCTGCTTCATGTATTCAGACTTCCATTTCATTGACGAACGAGGCGA
AF257191/-       GAAGTCTGCTTCATGTATTCAGACTTCCATTTCATTGACGAACGAGGCGA

NC_002022/-      GTCAATAATCGTAGAACTTGGTGATCCTAATGCACTTTTGAAGCACAGAT
X17336/-         GTCAATAGTCGTAGAACTTGGCGATCCAAATGCACTTTTGAAGCACAGAT
M81579/-         GTCAATAATAGTAGAGCTTGATGATCCAAATGCACTTTTGAAGCACAGAT
AF348174/-       GTCAATAGTGGTAGAACTTGATGATCCAAATGCACTTTTGAAGCACAGAT
```

FIG. 9A

```
AF257193/-      ATCAATAATTGTGGAATCTGGTGATCCGAATGCATTGTTGAAACACCGGT
AF257191/-      ATCAATAATTGTGGAATCTGGTGATCCAAATGCATTGTTGAAGCACAGGT

NC_002022/-     TTGAAATAATCGAGGGAAGAGATCGCACAATGGCCTGGACAGTAGTAAAC
X17336/-        TTGAAATAATCGAGGGAAGAGATCGCACAATAGCCTGGACAGTAATAAAC
M81579/-        TTGAAATAATAGAGGGAAGAGATCGCACAATGGCCTGGACAGTAGTAAAC
AF348174/-      TTGAAATAATAGAGGGAAGAGACCGCACAATGGCCTGGACAGTAGTAAAC
AF257193/-      TTGAAATAATTGAAGGAAGAGACCGAGCAATGGCCTGGACAGTGGTGAAT
AF257191/-      TTGAAATAATTGAAGGAAGAGACCGAGCAATGGCCTGGACAGTGGTGAAT

NC_002022/-     AGTATTTGCAACACTACAGGGGCTGAGAAACCAAAGTTTCTACCAGATTT
X17336/-        AGTATTTGCAACACTACAGGGGCTGAGAAACCAAAGTTTCTACCAGATTT
M81579/-        AGTATTTGCAACACTACAGGAGCTGAGAAACCGAAGTTTCTGCCAGATTT
AF348174/-      AGTATTTGCAACACCACAGGAGCTGAGAAACCGAAGTTTCTGCCAGATTT
AF257193/-      AGCATCTGCAACACCACAGGAGTCGATAAACCCAAATTTCTTCCGGATCT
AF257191/-      AGCATCTGCAACACAACAGGAGTCGATAAACCCAAATTTCTTCCGGATCT

NC_002022/-     GTATGATTACAAGGAAAATAGATTCATCGAAATTGGAGTAACAAGGAGAG
X17336/-        GTATGATTACAAGAAGAATAGATTCATCGAAATTGGAGTAACAAGGAGAG
M81579/-        GTATGATTACAAGGAGAATAGATTCATCGAGATTGGAGTGACAAGGAGGG
AF348174/-      GTATGATTACAAGGAGAATAGATTCATCGAGATTGGAGTGACAAGGAGAG
AF257193/-      ATACGACTACAAGGAAAACCGATTCACTGAAATTGGTGTGACACGGAGGG
AF257191/-      ATACGACTACAAGGAAAACCGATTCACTGAAATTGGTGTGACACGGAGGG

NC_002022/-     AAGTTCACATATACTATCTGGAAAAGGCCAATAAAATTAAATCTGAGAAA
X17336/-        AAGTTCACATATACTATCTGGAAAAGGCCAATAAAATTAAATCTGAGAAG
M81579/-        AAGTCCACATATACTATCTTGAAAAGGCCAATAAAATTAAATCTGAGAAG
AF348174/-      AAGTCCACATATACTACCTTGAAAAGGCCAATAAAATTAAATCTGAGAAT
AF257193/-      AAGTTCATATATATTACTTAGAGAAAGCTAACAAGATAAAATCCGAGAAA
AF257191/-      AAGTTCACATATATTACTTAGAAAAAGCTAACAAGATAAAATCCGAGAAA

NC_002022/-     ACACACATCCACATTTTCTCGTTCACTGGGGAAGAAATGGCCACAAAGGC
X17336/-        ACACACATCCACATTTTCTCATTCACTGGGGAGGAAATGGCCACAAAGGC
M81579/-        ACACACATCCACATTTTCTCATTCACTGGGGAAGAAATGGCCACAAAGGC
AF348174/-      ACACACATCCACATTTTCTCATTCACTGGGGAAGAAATGGCCACAAAGGC
AF257193/-      ACACATATCCACATCTTCTCATTCACTGGAGAAGAAATGGCCACTAAAGC
AF257191/-      ACACATATCCACATCTTTTCATTCACTGGAGAAGAAATGGCCACTAAAGC

NC_002022/-     CGACTACACTCTCGATGAAGAAAGCAGGGCTAGGATCAAAACCAGGCTAT
X17336/-        CGACTACACTCTCGATGAAGAAAGCAGGGCTAGGATCAAAACCAGGCTAT
M81579/-        CGACTACACTCTCGATGAGGAAAGCAGGGCTAGGATCAAGACCAGACTAT
AF348174/-      CGACTACACTCTCGATGAGGAAAGCAGGGCTAGGATCAAAACCAGACTAT
AF257193/-      TGACTACACCCTTGATGAAGAGAGCAGGGCAAGAATCAAAACCAGACTAT
AF257191/-      TGACTACACCCTTGATGAAGAGAGCAGGGCAAGAATAAAAACCAGACTAT
```

FIG. 9B

```
NC_002022/-     TCACCATAAGACAAGAAATGGCCAGCAGAGGCCTCTGGGATTCCTTTCGT
X17336/-        TCACCATAAGACAAGAAATGGCTAGCAGAGGCCTCTGGGATTCCTTTCGT
M81579/-        TCACCATAAGACAAGAAATGGCTAGCAGAGGCCTCTGGGATTCCTTTCGT
AF348174/-      TCACCATAAGACAAGAGATGGCCAACAGAGGCCTCTGGGATTCCTTTCGT
AF257193/-      TCACCATAAGACAGGAAATGGCAAGCAGGGGTCTATGGGACTCCTTTCGT
AF257191/-      TCACCATAAGACAGGAAATGGCAAGCAGGGGTCTATGGGATTCCTTTCGT

NC_002022/-     CAGTCCGAGAGAGGAGAAGAGACAATTGAAGAAAGGTTTGAAATCACAGG
X17336/-        CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
M81579/-        CAGTCCGAAAGAGGCGAAGAAACAATTGAAGAAAGATTTGAAATCACAGG
AF348174/-      CAGTCCGAAAGAGGCGAAGAAACAATTGAAGAAAGATTTGAAATCACAGG
AF257193/-      CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
AF257191/-      CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG

NC_002022/-     AACAATGCGCAAGCTTGCCGACCAAAGTCTCCCGCCGAACTTCTCCAGCC
X17336/-        AACAATGCGCAAGCTTGCCGACCAAAGTCTCCCGCCAAACTTCTCCAGCC
M81579/-        GACAATGCGCAGGCTCGCCGACCAAAGTCTCCCGCCGAACTTCTCCTGCC
AF348174/-      GACAATGCGCAGGCTTGCCGACCAAAGTCTCCCGCCGAACTTCTCCTGCC
AF257193/-      GACCATGCGTAGGCTTGCCGACCAAAGTCTCCCACCTAACTTCTCCAGCC
AF257191/-      GACCATGCGTAGGCTTGCCGACCAAAGTCTCCCACCTAACTTCTCCAGCC

NC_002022/-     TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAAGGGCTACATT
X17336/-        TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTACATT
M81579/-        TTGAGAATTTTAGAGCCTATGTGGATGGATTCGAACCCAACGGCTACATT
AF348174/-      TTGAGAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTACATT
AF257193/-      TTGAAAACTTTAGAGCCTATGTGGATGGATTTAAACCGAACGGCTGCATT
AF257191/-      TTGAAAACTTTAGAGCCTATGTGGATGGATTCAAACCGAACGGCTGCATT

NC_002022/-     GAGGGCAAGCTGTCTCAAATGTCCAAAGAAGTAAATGCTAGAATTGAACC
X17336/-        GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTAAATGCTAGAATTGAACC
M81579/-        GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTAAATGCTAAAATTGAGCC
AF348174/-      GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTGAATGCAAAAATTGAACC
AF257193/-      GAGGGCAAGCTTTCTCAAATGTCGAAAGAAGTGAACGCCAGAATTGAGCC
AF257191/-      GAGGGCAAGCTTTCTCAAATGTCGAAAGAAGTGAACGCCAGAATTGAGCC

NC_002022/-     TTTTTTGAAAACAACACCACGACCACTTAGACTTCCGAATGGGCCTCCCT
X17336/-        TTTTTTGAAATCAACACCACGACCACTTAGACTTCCGGATGGGCCTCCCT
M81579/-        TTTTCTGAAAACAACACCAAGACCAATTAAACTTCCGGATGGGCCTCCTT
AF348174/-      TTTTCTGAAAACAACACCAAGACCAATTAGACTTCCGGATGGGCCTCCTT
AF257193/-      ATTTCTGAAGACAACACCACGTCCTCTCAGATTGCCTGATGGACCTCCCT
AF257191/-      ATTTCTGAAGACAACACCACGTCCCCTCAGATTGCCTGATGGACCTCCCT
```

FIG. 9C

```
NC_002022/-     GTTCTCAGCGGTCCAAATTCCTGCTGATGGATGCCTTAAAATTAAGCATT
X17336/-        GTTCTCAGCGGTCCAAATTCCTGCTGATGGATGCCTTAAAATTAAGCATT
M81579/-        GCTCTCAGCGGTCCAAATTCCTGCTGATGGATGCTTTAAAATTAAGCATT
AF348174/-      GTTTTCAGCGGTCCAAATTCCTTCTGATGGATGCTTTAAAGTTAAGCATT
AF257193/-      GCTCCCAGCGGTCGAAATTCTTGCTGATGGATGCTCTGAAATTAAGCATT
AF257191/-      GCTCCCAGCGGTCGAAATTCTTGCTGATGGATGCTCTGAAATTAAGCATT

NC_002022/-     GAGGACCCAAGTCATGAAGGAGAGGGAATACCGCTATATGATGCAATCAA
X17336/-        GAGGACCCAAGTCATGAGGGAGAGGGGATACCGCTATATGATGCAATCAA
M81579/-        GAGGACCCAAGTCACGAAGGAGAGGGAATACCACTATATGATGCGATCAA
AF348174/-      GAGGATCCAAGTCACGAGGGGGAGGGAATACCACTATATGATGCGATCAA
AF257193/-      GAGGACCCGAGCCATGAGGGGGAGGGGATACCGCTATATGATGCGATCAA
AF257191/-      GAGGACCCGAGCCATGAGGGGGAGGGGATACCGCTATATGATGCGATAAA

NC_002022/-     ATGCATGAGAACATTCTTTGGATGGAAGGAACCCAATGTTGTTAAACCAC
X17336/-        ATGCATGAGAACATTCTTTGGATGGAAGGAACCCAATGTTGTTAAACCAC
M81579/-        GTGTATGAGAACATTCTTTGGATGGAAAGAACCCTATGTTGTTAAACCAC
AF348174/-      ATGCATGAGAACATTTTTTGGATGGAAAGAACCCTATATTGTTAAACCAC
AF257193/-      ATGCATGAAAACATTCTTTGGCTGGAGAGAGCCCAACATCATCAAACCAC
AF257191/-      ATGCATGAAAACATTCTTCGGCTGGAGAGAGCCCAACATCATCAAGCCAC

NC_002022/-     ACGAAAAGGGAATAAATCCAAATTATCTTCTGTCATGGAAGCAAGTACTG
X17336/-        ACGAAAAGGGAATAAATCCAAATTATCTTCTGTCATGGAAGCAAGTACTG
M81579/-        ACGATAAGGGAATAAATCCAAATTATCTGCTGTCATGGAAGCAATTACTG
AF348174/-      ACGAAAAGGGGATAAATCCAAATTATCTGCTGTCATGGAAGCAAGTACTG
AF257193/-      ACGAAAAAGGCATAAATCCAAATTATCTCCTGGCTTGGAAGCAGGTGCTG
AF257191/-      ACGAGAAGGGCATAAATCCCAATTATCTTCTGGCTTGGAAGCAGGTGCTG

NC_002022/-     GCAGAACTGCAGGACATTGAGAATGAGGAGAAAATTCCAAAGACTAAAAA
X17336/-        GCAGAACTGCAGGACATTGAGAATGAGGAGAAAATTCCAAGGACTAAAAA
M81579/-        GCAGAACTGCAGGACATTGAGAATGAGGAGAAGATTCCAAGAACCAAAAA
AF348174/-      GCAGAACTGCAGGACATTGAAAATGAGGAGAAAATTCCAAGAACTAAAAA
AF257193/-      GCAGAACTCCAGGATATTGAAAATGAGGATAAAATCCCAAAAACAAAGAA
AF257191/-      GCAGAACTCCAGGATATTGAAAATGAGGATAAAATCCCAAAAACAAAGAA

NC_002022/-     TATGAAAAAAACAAGTCAGCTAAAGTGGGCACTTGGTGAGAACATGGCAC
X17336/-        TATGAAGAAAACGAGTCAGTTAAAGTGGGCACTTGGTGAGAACATGGCAC
M81579/-        CATGAAGAAAACGAGTCAGCTAAAGTGGGCACTTGGTGAGAACATGGCAC
AF348174/-      CATGAAGAAAACGAGTCAGCTAAAGTGGGCACTTGGTGAGAACATGGCAC
AF257193/-      CATGAAGAAAACAAGCCAATTAATGTGGGCACTCGGAGAGAATATGGCAC
AF257191/-      CATGAAGAAAACAAGCCAATTAATGTGGGCACTCGGGGAGAATATGGCAC

NC_002022/-     CAGAAAAGGTAGACTTTGACGACTGTAAAGATGTAGGTGATTTGAAGCAA
X17336/-        CAGAAAAGGTAGACTTTGACGATTGTAAAGATGTAGGCGATTTGAAGCAA
```

FIG. 9D

```
M81579/-          CAGAGAAGGTAGACTTTGACGACTGTAGAGATATAAGCGATTTGAAGCAA
AF348174/-        CAGAGAAGGTAGACTTTGACAACTGTAGAGACGTAAGCGATTTGAAGCAA
AF257193/-        CGGAAAAAGTGGACTTTGAGGATTGCAAAGACATTGATGATCTGAAACAG
AF257191/-        CGGAAAAATTGGACTTTGAGGACTGCAAAGATATTGGCGATCTGAAACAG

NC_002022/-       TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
X17336/-          TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
M81579/-          TATGATAGTGATGAACCTGAATTAAGGTCACTTTCAAGCTGGATCCAGAA
AF348174/-        TATGATAGTGACGAACCTGAATTAAGGTCACTTTCAAGCTGGATCCAGAA
AF257193/-        TACCACAGTGATGAGCCAGAGCTTAGATCGCTAGCAAGCTGGATCCAGAA
AF257191/-        TATCAAAGTGATGAGCCAGAGCTCAGATCGATAGCAAGCTGGATCCAGAG

NC_002022/-       TGAGTTCAACAAGGCATGCGAACTGACAGATTCAAGCTGGATAGAGCTTG
X17336/-          TGAGTTCAACAAGGCATGTGAACTGACCGATTCAAGCTGGATAGAGCTCG
M81579/-          TGAGTTCAACAAGGCATGCGAGCTGACCGATTCAATCTGGATAGAGCTCG
AF348174/-        TGAGTTCAACAAGGCATGCGAGCTGACCGATTCAACTTGGATAGAGCTCG
AF257193/-        TGAGTTCAACAAGGCATGTGAATTGACCGATTCGAGCTGGATAGAACTTG
AF257191/-        TGAGTTCAACAAGGCATGTGAATTGACCGATTCGAGCTGGATAGAACTCG

NC_002022/-       ATGAGATTGGAGAAGATGTGGCTCCAATTGAACACATTGCAAGCATGAGA
X17336/-          ATGAGATTGGAGAAGATGCGGCTCCAATTGAACACATTGCAAGCATGAGA
M81579/-          ATGAGATTGGAGAAGATGTGGCTCCAATTGAACACATTGCAAGCATGAGA
AF348174/-        ATGAGATTGGAGAAGACGTGGCTCCAATTGAATACATTGCAAGCATGAGA
AF257193/-        ATGAGATAGGGGAAGATGTTGCCCCAATTGAGCACATTGCAAGTATGAGA
AF257191/-        ATGAGATAGGGGAAGATGTTGCCCCAATTGAGCACATTGCAAGCATGAGA

NC_002022/-       AGGAATTATTTCACATCAGAGGTGTCTCACTGCAGAGCCACAGAATACAT
X17336/-          AGGAATTATTTCACAGCAGAGGTGTCTCATTGCAGAGCCACAGAATACAT
M81579/-          AGGAATTACTTCACAGCAGAGGTGTCTCAGTGCAGAGCCACAGAATATTAT
AF348174/-        AGGAATTACTTCACAGCAGAGGTGTCCCATTGCAGAGCCACAGAATATTAT
AF257193/-        AGGAACTACTTCACAGCGGAGGTGTCCCATTGCAGGGCTACTGAGTACAT
AF257191/-        AGGAACTACTTCACAGCGGAAGTGTCTCATTGCAGGGCCACTGAGTACAT

NC_002022/-       AATGAAGGGGGTGTACATCAATACTGCCTTACTTAATGCATCTTGTGCAG
X17336/-          AATGAAGGGGGTGTACATCAATACTGCCTTGCTTAATGCATCCTGTGCAG
M81579/-          AATGAAGGGGGTATACATTAATACTGCCTTGCTTAATGCATCCTGTGCAG
AF348174/-        AATGAAGGGGGTATACATTAATACTGCCTTGCTTAATGCATCCTGTGCAG
AF257193/-        AATGAAGGGGGTTTACATAAATACAGCTTTGCTCAATGCATCTTGTGCAG
AF257191/-        AATGAAGGGGGTTTACATAAATACAGCTTTGCTCAATGCATCTTGTGCAG

NC_002022/-       CAATGGATGATTTCCAATTAATTCCAATGATAAGCAAGTGTAGAACTAAG
X17336/-          CAATGGATGATTTCCAATTAATTCCAATGATAAGCAAGTGTAGAACTAAG
M81579/-          CAATGGACGATTTCCAACTAATTCCCATGATAAGCAAATGTAGAACTAAA
AF348174/-        CAATGGACGATTTCCAACTAATTCCCATGATAAGCAAGTGTAGAACTAAA
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FIG. 9E

```
AF257193/-      CCATGGATGACTTCCAACTGATTCCAATGATAAGCAAATGCAGAACAAAA
AF257191/-      CCATGGATGACTTCCAACTGATTCCAATGATAAGCAAATGCAGAACAAAA

NC_002022/-     GAGGGAAGGCGAAAGACCAACTTGTATGGTTTCATCATAAAAGGAAGATC
X17336/-        GAGGGAAGGCGAAAGACCAATTTGTACGGTTTCATCATAAAAGGAAGATC
M81579/-        GAGGGAAGGCGAAAGACCAATTTATATGGTTTCATCATAAAAGGAAGATC
AF348174/-      GAAGGAAGGCGAAAGACCAATTTATATGGCTTCATCATAAAAGGAAGATC
AF257193/-      GAAGGAAGGAGGAGGACAAACCTGTATGGGTTCATTGTAAAAGGAAGGTC
AF257191/-      GAAGGAAGAAGGAAGACAAACCTGTATGGGTTCATTATAAAAGGAAGGTC

NC_002022/-     CCACTTAAGGAATGACACCGACGTGGTAAACTTTGTGAGCATGGAGTTTT
X17336/-        CCACTTAAGGAATGACACCGATGTGGTAAACTTTGTGAGCATGGAGTTTT
M81579/-        TCACTTAAGGAATGACACCGACGTGGTAAACTTTGTGAGCATGGAGTTTT
AF348174/-      TCACTTAAGGAATGACACCGACGTGGTAAACTTTGTGAGCATGGAGTTTT
AF257193/-      CCATTTGAGAAATGATACTGACGTGGTGAACTTTGTGAGTATGGAATTCT
AF257191/-      CCATTTGAGAAATGATACTGACGTGGTGAACTTTGTGAGTATGGAATTCT

NC_002022/-     CTCTCACTGACCCAAGACTTGAACCACACAAATGGGAGAAGTACTGTGTT
X17336/-        CCTCACTGACCCAAGACTTGAACCACACAAATGGGAGAAGTACTGTGTT
M81579/-        CTCTCACTGACCCAAGACTTGAGCCACACAAATGGGAGAAGTACTGTGTT
AF348174/-      CTCTCACTGACCCGAGACTTGAGCCACACAAATGGGAGAAATACTGTGTC
AF257193/-      CCCTTACTGACCCAAGGCTGGAGCCACACAAATGGGAAAAGTACTGTGTT
AF257191/-      CCCTTACTGACCCAAGGCTGGAGCCACACAAATGGGAAAAGTACTGTGTT

NC_002022/-     CTTGAGATAGGAGATATGCTTCTAAGAAGTGCCATAGGCCAGGTTTCAAG
X17336/-        CTTGAGGTAGGAGATATGCTTCTAAGAAGTGCCATAGGCCATGTGTCAAG
M81579/-        CTTGAGATAGGAGATATGCTACTAAGAAGTGCCATAGGCCAGGTGTCAAG
AF348174/-      CTTGAGATAGGAGATATGCTACTAAGAAGTGCTATAGGCCAGATGTCAAG
AF257193/-      CTTGAAATAGGGGAAATGCTCTTGCGGACTGCAATAGGTCAAGTGTCAAG
AF257191/-      CTTGAAGTAGGGGAAATGCTCTTGCGGACTGCAATAGGCCAGGTGTCAAG

NC_002022/-     GCCCATGTTCTTGTATGTGAGGACAAATGGAACCTCAAAAATTAAAATGA
X17336/-        GCCTATGTTCTTGTATGTGAGGACAAATGGAACCTCAAAAATTAAAATGA
M81579/-        GCCCATGTTCTTGTATGTGAGGACAAATGGAACATCAAAGATTAAAATGA
AF348174/-      GCCTATGTTCTTGTATGTGAGAACAAATGGAACATCAAAGATTAAAATGA
AF257193/-      GCCCATGTTCCTGTATGTGAGAACCAACGGAACCTCAAAAATTAAGATGA
AF257191/-      GCCCATGTTCCTGTATGTGAGAACTAACGGAACCTCCAAAATTAAGATGA

NC_002022/-     AATGGGGAATGGAGATGAGGCGTTGTCTCCTCCAGTCACTTCAACAAATT
X17336/-        AATGGGGGATGGAAATGAGGCGTTGCCTCCTTCAGTCACTTCAACAAATC
M81579/-        AATGGGGAATGGAGATGAGGCGTTGCCTCCTTCAGTCACTCCAACAAATC
AF348174/-      AATGGGGAATGGAGATGAGGCGTTGCCTCCTTCAGTCACTCCAACAAATC
AF257193/-      AATGGGGGATGGAAATGAGGCGCTGCCTTCTTCAATCTCTTCAACAGATT
AF257191/-      AATGGGGGATGGAAATGAGACGCTGCCTTCTTCAATCTCTTCAACAGATT
```

FIG. 9F

```
NC_002022/-     GAGAGTATGATTGAAGCTGAGTCCTCTGTCAAAGAGAAAGACATGACCAA
X17336/-        GAGAGTATGATTGAAGCTGAGTCCTCTGTCAAGGAGAAAGACATGACCAA
M81579/-        GAGAGTATGATTGAAGCCGAGTCCTCTGTCAAGGAGAAAGACATGACCAA
AF348174/-      GAGAGTATGATTGAAGCAGAGTCATCTGTCAAAGAGAAAGACATGACCAA
AF257193/-      GAGAGCATGATCGAGGCTGAGTCTTCTATCAAAGAGAAAGACATGACCAA
AF257191/-      GAGAGCATGATCGAGGCTGAGTCTTCTATCAAAGAGAAAGACATGACCAA

NC_002022/-     AGAGTTCTTTGAGAACAAATCAGAAACATGGCCCATTGGAGAGTCTCCCA
X17336/-        AGAGTTCTTTGAAAACAAATCAGAAACATGGCCCGTTGGAGAGTCCCCCA
M81579/-        AGAGTTTTTCGAGAATAAATCAGAAACATGGCCCATTGGAGAGTCCCCCA
AF348174/-      AGAGTTTTTTGAGAATAAATCAGAAACATGGCCCATTGGGGAGTCCCCCA
AF257193/-      AGAATTCTTTGAAAACAGATCGGAGACATGGCCAATTGGAGAGTCACCTA
AF257191/-      AGAATTCTTTGAAAACAGATCGGAGACATGGCCAATTGGAGAGTCACCTA

NC_002022/-     AAGGAGTGGAGGAAAGTTCCATTGGGAAGGTCTGCAGGACTTTATTAGCA
X17336/-        AAGGAGTGGAGGAAGGTTCCATTGGGAAGGTCTGCAGAACTTTATTGGCA
M81579/-        AAGGAGTGGAAGAAGGTTCCATTGGGAAGGTCTGCAGGACTTTATTAGCC
AF348174/-      AGGGAGTGGAAGATGGTTCCATTGGGAAGGTCTGCAGGACTTTATTGGCC
AF257193/-      AGGGAGTGGAGGAAGGCTCCATCGGGAAGGTGTGCAGAACCTTACTAGCA
AF257191/-      AGGGAGTGGAGGAAGGCTCAATCGGGAAGGTGTGCAGAACCTTACTAGCA

NC_002022/-     AAGTCGGTATTTAACAGCTTGTATGCATCTCCACAACTAGAAGGATTTTC
X17336/-        AAGTCGGTATTCAACAGCTTGTATGCATCTCCACAACTGGAAGGATTTTC
M81579/-        AAGTCGGTATTCAATAGCCTGTATGCATCTCCACAATTAGAAGGATTTTC
AF348174/-      AAGTCGGTATTCAATAGCCTGTATGCATCCCGCAATTGGAAGGGTTTTC
AF257193/-      AAATCTGTGTTCAACAGCCTATATTTCATCTCCACAACTCGAAGGATTTTC
AF257191/-      AAATCTGTGTTCAACAGCCTATATTCATCTCCACAACTCGAAGGATTTTC

NC_002022/-     AGCTGAATCAAGAAAACTGCTTCTTATCGTTCAGGCTCTTAGGGACAATC
X17336/-        AGCTGAATCAAGAAAACTGCTTCTTATCGTTCAGGCTCTTAGGGACAACC
M81579/-        AGCTGAATCAAGAAAACTGCTTCTTGTCGTTCAGGCTCTTAGGGACAATC
AF348174/-      AGCTGAGTCAAGAAAACTGCTTCTTGTCGTTCAGGCTCTTAAGGACAATC
AF257193/-      AGCTGAATCGAGAAAACTACTACTCATTGTTCAAGCACTTAGGGACAACC
AF257191/-      AGCTGAATCGAGAAAACTACTACTCATTGTTCAAGCACTTAGGGACAACC

NC_002022/-     TGGAACCTGGGACCTTTGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
X17336/-        TGGAACCTGGGACCTTTGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
M81579/-        TTGAACCTGGGACCTTTGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
AF348174/-      TTGAACCTGGAACCTTTGATCTTGAGGGGCTATATGAAGCAATTGAGGAG
AF257193/-      TGGAACCTGGAACCTTCGATCTTGAAGGGCTATATGGAGCAATTGAGGAG
AF257191/-      TGGAACCTGGAACCTTTGATCTTGAAGGGCTATATGGAGCAATTGAGGAG
```

FIG. 9G

```
NC_002022/-     TGCCTAATTAATGATCCCTGGGTTTTGCTTAATGCTTCTTGGTTCAACTC
X17336/-        TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCTTCTTGGTTCAACTC
M81579/-        TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCGTCTTGGTTCAACTC
AF348174/-      TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCGTCGTGGTTCAACTC
AF257193/-      TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC
AF257191/-      TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC

NC_002022/-     GTTCCTTACACATGCATTGAGTTAGTTGTGGCAGTGCTACTATTTGCTAT
X17336/-        CTTCCTCACACATGCATTGAGATAGTTGTGGCAATGCTACTATTTGCTAT
M81579/-        CTTCCTAACACATGCATTAAGATAGTTGTGGCAATGCTACTATTTGCTAT
AF348174/-      CTTCCTAACACATGCATTAAGATAGTTGTGGCAATGCTACTATTTGCTAT
AF257193/-      CTTCCTCACACATGCACTAAGATAGTTGTGGCAATGCTACTATTTGCTAT
AF257191/-      CTTCCTCACACATGCACTAAAATAGTTGTGGCAATGCTACTATTTGCTAT

NC_002022/-     CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--    (SEQ ID NO: 121)

X17336/-        CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--    (SEQ ID NO: 122)

M81579/-        CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--    (SEQ ID NO: 123)

AF348174/-      CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--    (SEQ ID NO: 124)

AF257193/-      CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--    (SEQ ID NO: 125)

AF257191/-      CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--    (SEQ ID NO: 126)
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FIG. 9H

CLUSTAL W(1.4) multiple sequence alignment

Shaded area: selected siRNA sequence.

NC_002022	A/Puerto Rico/8/34	H1N1	1934	2233 nt
X17336	A/WSN/33	H1N1	1933	2233 nt
M21850	A/chicken/FPV/Rostock/34	H7N1	1934	2233 nt
AF156457	A/turkey/California/189/66	H9M2	1966	2140 nt
M26087	A/Equine/London/1416/73	H7N7	1973	2233 nt
M26088	A/gull/Maryland/704/77	H13N6	1977	2233 nt
AF222820	A/swine/Hong Kong/9/98	H9N2	1998	1635 nt

```
NC_002022/-          AGCGAAAGCAGGTACTGATCCAAAATGGAAGATTTTGTGCGACAATGCTT
X17336/-             AGCGAAAGCAGGTACTGATTCAAAATGGAAGATTTTGTGCGACAATGCTT
M21850/-             AGCGAAAGCAGGTACTGATCCAAAATGGAAGAATTTGTGCGACAATGCTT
AF156457/-           ----------------------ATGGAAGACTTCGTGCGACAATGCTT
M26087/-             AGCAAAAGCAGGTACTGATCCAAAATGGAAGACTTTGTGCGACAATGCTT
M26088/-             AGCAAAAGCAGGTACTGATTCAAAATGGAAGACTTTGTGCGACAATGCTT
AF222820/-           --------------------------------------------------

NC_002022/-          CAATCCGATGATTGTCGAGCTTGCGGAAAAAACAATGAAAGAGTATGGGG
X17336/-             CAATCCGATGATTGTCGAGCTTGCGGAAAAGGCAATGAAAGAGTATGGAG
M21850/-             CAATCCAATGATCGTCGAGCTTGCGGAAAAGACAATGAAAGAATATGGAG
AF156457/-           CAATCCAATGATTGTCGAGCTTGCGGAAAAGGCAATGAAAGAATATGGAG
M26087/-             CAATCCAATGATCGTCGAGCTTGCGGAAAAGGCGATGAAAGAATATGGAG
M26088/-             CAATCCAATGATCGTCGAGCTTGCGGAAAAGGCAATGAAAGAATATGGAG
AF222820/-           --------------------------------------------------

NC_002022/-          AGGACCTGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
X17336/-             AGGACCTGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
M21850/-             AGGACCCGAAGATTGAAACAAACAAATTCGCAGCAATATGCACACATTTG
AF156457/-           AGGGCCCGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCATTTG
M26087/-             AGGACCCGAAAATTGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
M26088/-             AGGATCCAAAAATCGAGACAAACAAATTCGCTGCAATATGCACACACCTG
AF222820/-           --------------------------------------------------

NC_002022/-          GAAGTATGCTTCATGTATTCAGATTTCCACTTCATCAATGAGCAAGGCGA
X17336/-             GAAGTGTGCTTCATGTATTCAGATTTTCACTTCATCGATGAGCAAGGCGA
M21850/-             GAAGTGTGTTTCATGTATTCAGATTTCCACTTTATTGATGAACGGGGAGA
AF156457/-           GAAGTGTGTTTCATGTATTCAGACTTTCACTTCATCGATGAGCGAGGCGA
M26087/-             GAAGTCTGCTTCATGTACTCGGATTTCCACTTTATTAATGAACTGGGCGA
M26088/-             GAAGTGTGTTTCATGTATTCAGACTTCCATTTCATTGATGAACGGGGTGA
AF222820/-           --------------------------------------------------

NC_002022/-          GTCAATAATCGTAGAACTTGGTGATCCTAATGCACTTTTGAAGCACAGAT
```

FIG. 10A

```
X17336/-          GTCAATAGTCGTAGAACTTGGCGATCCAAATGCACTTTTGAAGCACAGAT
M21850/-          GTCAAAGATTGTAGAATCTGGTGACCCAAATGCACTCTTGAAGCACCGAT
AF156457/-        ATCAATAATTGTAGAATCCGGAGATCCGAATGCCCTCTTGAAGCACAGAT
M26087/-          GTCAGTGATCATAGAGTCTGGTGATCCAAATGCTCTTTTGAAGCACAGAT
M26088/-          GTCGATAATTGTTGAGTCTGGTGATCCAAATGCACTCTTAAAACATCGAT
AF222820/-        --------------------------------------------------

NC_002022/-       TTGAAATAATCGAGGGAAGAGATCGCACAATGGCCTGGACAGTAGTAAAC
X17336/-          TTGAAATAATCGAGGGAAGAGATCGCACAATAGCCTGGACAGTAATAAAC
M21850/-          TTGAGATAATTGAAGGAAGAGATCGCACGATGGCCTGGACGGTGGTGAAT
AF156457/-        TTGAAATAATTGAGGGAAGAGATCGCACAATGGCCTGGACAGTGGTGAAC
M26087/-          TTGAAATCATTGAAGGGAGAGATCGAACAATGGCATGGACAGTAGTGAAC
M26088/-          TTGAAATAATCGAAGGAAGAGACCGTACTATGGCCTGGACAGTGGTGAAT
AF222820/-        --------------------------------------------------

NC_002022/-       AGTATTTGCAACACTACAGGGGCTGAGAAACCAAAGTTTCTACCAGATTT
X17336/-          AGTATTTGCAACACTACAGGGGCTGAGAAACCAAAGTTTCTACCAGATTT
M21850/-          AGCATTTGCAATACTACAGGGGTTGAGAAACCCAAGTTCCTTCCGGATTT
AF156457/-        AGCATCTGTAACACTACAGGGGTTGAGAAGCCAAGGTTTCTCCCAGATCT
M26087/-          AGTATCTGCAACACCACAAGAGCTGAAAAACCCAAGTTCCTCCCAGATTT
M26088/-          AGCATTTGCAACACCACAGGAGTTGAGAAGCCAAAGTTTCTTCCGGACTT
AF222820/-        --------------------------------------------------

NC_002022/-       GTATGATTACAAGGAAAATAGATTCATCGAAATTGGAGTAACAAGGAGAG
X17336/-          GTATGATTACAAGAAGAATAGATTCATCGAAATTGGAGTAACAAGGAGAG
M21850/-          GTATGATTATAAGGAGAACCGATTCATTGAAATTGGAGTGACAAGAAGGG
AF156457/-        ATATGACTACAAGGAGAACAGGTTCATTGAGATTGGAGTGACAAGGAGAG
M26087/-          GTACGACTATAAAGAGAACAGGTTTGTTGAAATTGGTGTGACAAGGAGAG
M26088/-          ATATGATTATAAAGAAAATCGTTTCATTGAAATTGGAGTGACAAGGAGGG
AF222820/-        --------------------------------------------------

NC_002022/-       AAGTTCACATATACTATCTGGAAAAGGCCAATAAAATTAAATCTGAGAAA
X17336/-          AAGTTCACATATACTATCTGGAAAAGGCCAATAAAATTAAATCTGAGAAG
M21850/-          AGGTCCACATATACTACTTAGAAAAAGCCAATAAGATAAAATCTGAGAAG
AF156457/-        AAGTCCACATATACTACCTGGAAAAGGCCAATAAAATAAAGTCTGAGAAG
M26087/-          AAGTTCACATATACTACTTGGAGAAAGCCAACAAAATAAAGTCTGAGAAA
M26088/-          AGGTCCATATATACTATCTAGAAAAGGCCAATAAGATAAAGTCTGAGAAG
AF222820/-        --------------------------------------------------

X17336/-          ACACACATCCACATTTTCTCATTCACTGGGGAGGAAATGGCCACAAAGGC
M21850/-          ACACACATCCACATCTTCTCATTCACTGGGGAAGAAATGGCCACTAAGGC
NC_002022/-       ACACACATCCACATTTTCTCGTTCACTGGGGAAGAAATGGCCACAAAGGC
AF156457/-        ACACATATCCACATCTTCTCGTTCACAGGAGAAGAGATGGCCACAAAGGC
M26087/-          ACACATATTCACATTTTCTCATTTACAGGAGAGGAAATGGCTACAAAAGC
M26088/-          ACACACATCCATATCTTTTCATTCACTGGAGAAGAAATGGCCACAAAAGC
```

FIG. 10B

```
AF222820/-          --------------------------------------------------

NC_002022/-         CGACTACACTCTCGATGAAGAAAGCAGGGCTAGGATCAAAACCAGGCTAT
X17336/-            CGACTACACTCTCGATGAAGAAAGCAGGGCTAGGATCAAAACCAGGCTAT
M21850/-            GGACTACACTCTTGATGAAGAGAGCAGAGCAAGGATCAAAACCAGGCTAT
AF156457/-          TGACTACACTCTTGATGAAGAAAGTAGGGCCAGAATCAAAACTAGACTGT
M26087/-            GGATTATACCCTTGATGAAGAAAGTAGAGCCAGGATCAAAACCAGACTAT
M26088/-            AGACTACACTCTTGATGAAGAGAGTAGAGCAAGGATCAAAACCAGACTAT
AF222820/-          ----------------AGCAAAAGCAGGGCAAGGATCAAAACTAGGCTGT

NC_002022/-         TCACCATAAGACAAGAAATGGCCAGCAGAGGCCTCTGGGATTCCTTTCGT
X17336/-            TCACCATAAGACAAGAAATGGCTAGCAGAGGCCTCTGGGATTCCTTTCGT
M21850/-            TCACCATAAGACAAGAAATGGCCAGTAGAGGCCTCTGGGATTCCTTTCGT
AF156457/-          TCACCATAAGGCAGGAAATGGCCAGTAGAGGTCTCTGGGATTCCTTTCGT
M26087/-            TCACCATAAGACAAGAAATGGCCAGCAGAGGCCTTTGGGACTCCTTTCGT
M26088/-            TCACTATAAGACAAGAAATGGCCAGTAGAGGTCTCTGGGATTCCTTTCGT
AF222820/-          TCACCATAAGACAGGAACTGGCTAGCAGGGGTCTATGGGATTCCTTTCGT

NC_002022/-         CAGTCCGAGAGAGGAGAAGAGACAATTGAAGAAAGGTTTGAAATCACAGG
X17336/-            CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
M21850/-            CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
AF156457/-          CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
M26087/-            CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
M26088/-            CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATTACAGG
AF222820/-          CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG

NC_002022/-         AACAATGCGCAAGCTTGCCGACCAAAGTCTCCCGCCGAACTTCTCCAGCC
X17336/-            AACAATGCGCAAGCTTGCCGACCAAAGTCTCCCGCCAAACTTCTCCAGCC
M21850/-            AACCATGCGCAGGCTTGCCGAACAAAGTCTCCCACCGAACTTCTCCAGCC
AF156457/-          AACAATGCGCAGGCTTGCCGACCAAAGTCTCCCACCGAACTTCTCCAGCC
M26087/-            GACAATGCGCAGGCTTGCCGATTACAGTCTCCCACCGAACTTCTCCAGCC
M26088/-            AACCATGCGCAGGCTCGCCGACCAAAGTCTCCCACCGAACTTCTCCAGCC
AF222820/-          AACAATGCGCAGGCTTGCCGACCAAAGTCTCCCACCGAATTTCTCCAGCC

NC_002022/-         TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTACATT
X17336/-            TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTACATT
M21850/-            TTGAAAACTTTAGAGCCTATGTGGATGGATTCAAACCGAACGGCTGCATT
AF156457/-          TTGAAAACTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTGCATT
M26087/-            TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTGCATT
M26088/-            TTGAAAACTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTGCATT
AF222820/-          TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTGCATT

NC_002022/-         GAGGGCAAGCTGTCTCAAATGTCCAAAGAAGTAAATGCTAGAATTGAACC
X17336/-            GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTAAATGCTAGAATTGAACC
```

FIG. 10C

```
M21850/-        GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTAAATGCAAGAATCGAGCC
AF156457/-      GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTGAATGCAAGAATTGAACC
M26087/-        GAGAGCAAGCTTTCTCAAATGTCAAAAGAAGTAAATACCAGAATCGAGCC
M26088/-        GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTAAATGCAAGAATTGAACC
AF222820/-      GAGGGCAAGCTTTCTCAGATGTCAAAAGAAGTAACGGCCAGAATTGAGCC

NC_002022/-     TTTTTTGAAAACAACACCACGACCACTTAGACTTCCGAATGGGCCTCCCT
X17336/-        TTTTTTGAAATCAACACCACGACCACTTAGACTTCCGGATGGGCCTCCCT
M21850/-        ATTCTTGAAGACAACACCACGCCCTCTCAGATTACCTGATGGGCCTCCCT
AF156457/-      CTTTTTGAAGACAACACCACGCCCACTCAAGCTACCAGATGGGCCTCCCT
M26087/-        ATTTTCAAAGACAACACCCCGGCCACTCAGGACACCGGGTGGTCCACCCT
M26088/-        ATTTTTGAAGACAACACCACGCCTCTCAGATTACCAGAAGGGCCTCCCT
AF222820/-      CTTTCTTAAAACAACACCACGTCCTCTAAGACTGCCGGGTGGACCTCCCT

NC_002022/-     GTTCTCAGCGGTCCAAATTCCTGCTGATGGATGCCTTAAAATTAAGCATT
X17336/-        GTTCTCAGCGGTCCAAATTCCTGCTGATGGATGCCTTAAAATTAAGCATT
M21850/-        GTTCTCAGCGGTCAAAATTCCTACTGATGGATGCTCTGAAATTAAGCATT
AF156457/-      GCTCCCAGCGGTCCAAATTCCTGCTAATGGACGCTTTGAAATTAAGCATT
M26087/-        GTTATCAGCGATCCAAATTCTTGCTGATGGATGCTCTGAAATTTAGCATT
M26088/-        GCTCTCAGCGGTCAAAATTTCTGTTGATGGATGCTCTGAAGCTTAGCATT
AF222820/-      GTTCCCAAAGGTCAAAATTCTTACTGATGGATGCTCTGAAATTAAGCATT

NC_002022/-     GAGGACCCAAGTCATGAAGGAGAGGGAATACCGCTATATGATGCAATCAA
X17336/-        GAGGACCCAAGTCATGAGGGAGAGGGGATACCGCTATATGATGCAATCAA
M21850/-        GAAGACCCAAGTCATGAGGGGAGGGGATACCACTACATGATGCAATCAA
AF156457/-      GAGGACCCAAGCCATGAAGGAGAAGGGATACCGCTATATGATGCAATCAA
M26087/-        GAGGATCCAAGTCACGAGGGAGAGGGAATACCGCTGTATGATGCCATCAA
M26088/-        GAAGACCCGAGTCATGAGGGTGAGGGAATACCACTGTATGATGCTATCAA
AF222820/-      GAGGACCCGAGTCATGAGGGAGAGGGGATACCGCTGTATGATGCGATCAA

NC_002022/-     ATGCATGAGAACATTCTTTGGATGGAAGGAACCCAATGTTGTTAAACCAC
X17336/-        ATGCATGAGAACATTCTTTGGATGGAAGGAACCCAATGTTGTTAAACCAC
M21850/-        ATGCATGAAGACATTCTTTGGCTGGAAAGAGCCCAATATTGTCAAACCGC
AF156457/-      ATGCATGAAAACATTCTTTGGGTGGAAAGAACCCAATATTGTTAAACCAC
M26087/-        ATGCATGAAAACCTTCTTTGGATGGAAAGAGCCCAATATTGTTAAACCAC
M26088/-        ATGTATGAAGACCTTTTTTGGCTGGAAAGAGCCCAACATTGTCAAGCCAC
AF222820/-      ATGCATGAAAACATTTTTCGGCTGGAAAGAGCCCAAAATTATCAAGTCAC

NC_002022/-     ACGAAAAGGGAATAAATCCAAATTATCTTCTGTCATGGAAGCAAGTACTG
X17336/-        ACGAAAAGGGAATAAATCCAAATTATCTTCTGTCATGGAAGCAAGTACTG
M21850/-        ATGAGAAGGGCATAAATCCCAACTATCTCCTGGCTTGGAACCAGGTGCTA
AF156457/-      ATGAAAAAGGAATAAATCCGAATTACCTCTTGGCATGGAAACAAGTACTA
M26087/-        ATGAAAAGGGTATAAACCCAAACTATCTCCAGGCTTGGAAGCAAGTGTTA
M26088/-        ATGAGAGGGGCATAAACCCTAATTATCTCCTGGCTTGGAAGCAAGTGCAA
AF222820/-      ATGAGAAGGGTATAAACCCAAATTATCTCCTAGCTTGGAAGCAGGTGCTG
```

FIG. 10D

```
NC_002022/-     GCAGAACTGCAGGACATTGAGAATGAGGAGAAAATTCCAAAGACTAAAAA
X17336/-        GCAGAACTGCAGGACATTGAGAATGAGGAGAAAATTCCAAGGACTAAAAA
M21850/-        GCAGAACTGAAGGATATTGAGAATGAGGAGAAAATTCCAAAAACAAAAA
AF156457/-      GCGGAACTACAGGATCTTGAAAATGAAGAGAAAATTCCAAAGACTAAAAA
M26087/-        GCAGAACTACAGGACCTCGAAAACGAAGAAAAAATCCCTAAGACCAAGAA
M26088/-        GCAGAACTGCAGGATATTGAAAATGAAGACAAGATTCCAAAGACAAAAAA
AF222820/-      GCAGAGCTCCAGGACATTGAAAATGATGAAAAGATCCCAAAAACAAAGAA

NC_002022/-     TATGAAAAAAACAAGTCAGCTAAAGTGGGCACTTGGTGAGAACATGGCAC
X17336/-        TATGAAGAAAACGAGTCAGTTAAAGTGGGCACTTGGTGAGAACATGGCAC
M21850/-        TATGAAGAAAACAAGCCAGTTAAAGTGGGCACTTGGTGAGAACATGGCAC
AF156457/-      CATGAAGAAAACAAGCCAATTAAAGTGGGCACTTGGTGAGAATATGGCAC
M26087/-        TATGAAAAAAACAAGTCAATTGAAATGGGCACTTGGTGAGAATATGGCGC
M26088/-        CATGAAGAAAACAAGCCAATTAAAGTGGGCACTTGGTGAGAACATGGCAC
AF222820/-      CATGAAGAAAACAAGCCAATTAAAGTGGGCATTAGGTGAGAACATGGCAC

NC_002022/-     TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
X17336/-        CAGAAAAGGTAGACTTTGACGATTGTAAAGATGTAGGCGATTTGAAGCAA
M21850/-        CAGAGAAAGTAGACTTTGAGGATTGCAAGGACATTAGCGATCTGAAGCAG
NC_002022/-     TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
AF156457/-      CAGAAAAAGTGGATTTTGAGGACTGCAAGGATGTCAGCGATCTGAAGCAA
M26087/-        CAGAGAAAGTGGATTTTGAGGATTGTAAAGACATCAGTGATTTGAAACAG
M26088/-        CAGAGAAAGTGGACTTTGAAGATTGCAAGGATGTCAGCGATTTGAAACAG
AF222820/-      CAGAGAAAGTGGACTTTGAGGATTGCAAAGACGTTAGTGACCTGAAACAA

NC_002022/-     TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
X17336/-        TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
M21850/-        TATGACAGTGATGAGCCAGAACAGAGATCACTAGCGAGTTGGATCCAGAG
AF156457/-      TATGACAGTGATGAACCGGAACCGAGATCGCTTGCAAGTTGGATTCAGAG
M26087/-        TATGACAGTGATGAGCCAGAAACAAGGTCCCTTGCAAGTTGGATTCAAAG
M26088/-        TATGACAGCGATGAGCCAGAACAAAGGTCGCTAGCAAGTTGGGTCCAAAG
AF222820/-      TATGATAGTGATGAACCAGAGCCCAAATCGCTAGCAAGTTGGATCCAGAG

NC_002022/-     TGAGTTCAACAAGGCATGCGAACTGACAGATTCAAGCTGGATAGAGCTTG
X17336/-        TGAGTTCAACAAGGCATGTGAACTGACCGATTCAAGCTGGATAGAGCTCG
M21850/-        TGAATTCAACAAAGCATGTGAGCTGACCGATTCAGGTTGGATAGAACTTG
AF156457/-      TGAGTTCAATAAGGCGTGTGAACTGACTGATTCAAGCTGGATAGAGCTTG
M26087/-        TGAGTTCAACAAAGCTTGTGAGCTGACAGATTCAAGCTGGATAGAGCTCG
M26088/-        TGAATTCAACAAAGCTTGTGAATTGACTGATTCAAGCTGGATAGAACTCG
AF222820/-      TGAATTTTAACAAGGCATGTGAGTTGACCGATTCAAGCTGGGTAGAACTTG

NC_002022/-     ATGAGATTGGAGAAGATGTGGCTCCAATTGAACACATTGCAAGCATGAGA
X17336/-        ATGAGATTGGAGAAGATGCGGCTCCAATTGAACACATTGCAAGCATGAGA
```

FIG. 10E

```
M21850/-          ATGAAATAGGAGAAGATGTAGCCCCAATCGAGCACATTGCAAGTATGAGG
AF156457/-        ACGAGATTGGGGAAGATGTTGCCCCAATTGAGCACATTGCAAGCATGAGG
M26087/-          ATGAAATTGGGGAGGATGTTGCCCCAATAGAACACATTGCGAGCATGAGG
M26088/-          ATGAAATAGGGGAAAATGTCGCCCCAATCGAGCATATTGCAAGCATGAGG
AF222820/-        ATGAAATAGGAGAAGATGTTGCTCCAATCGAGCACATTGCGAGTATGAGA

NC_002022/-       AGGAATTATTTCACATCAGAGGTGTCTCACTGCAGAGCCACAGAATACAT
X17336/-          AGGAATTATTTCACAGCAGAGGTGTCTCATTGCAGAGCCACAGAATACAT
M21850/-          AGAAACTATTTCACAGCGGAAGTGTCTCACTGCAGGGCAACGGAGTACAT
AF156457/-        AGGAATTATTTCACAGCGGAGGTGTCTCATTGTAGAGCCACAGAATACAT
M26087/-          AGGAATTATTTTACTGCTGAGGTTTCCCATTGTAGAGCAACTGAATATAT
M26088/-          AGGAATTATTTTACAGCTGAAGTGTCTCACTGCAGGGCAACAGAGTACAT
AF222820/-        AGGAATTACTTCACAGCAGAAGTGTCACACTGCCGGGCTACTGAGTATAT

NC_002022/-       AATGAAGGGGGTGTACATCAATACTGCCTTACTTAATGCATCTTGTGCAG
X17336/-          AATGAAGGGGGTGTACATCAATACTGCCTTGCTTAATGCATCCTGTGCAG
M21850/-          AATGAAAGGGGTATACATAAACACGGCCTTGCTCAATGCATCTTGTGCAG
AF156457/-        AATGAAAGGGGTATACATCAATACTGCCTTGCTCAATGCATCCTGTGCGG
M26087/-          AATGAAGGGAGTATACATCAACACTGCTCTACTCAATGCATCCTGCGCTG
M26088/-          AATGAAGGGAGTGTACATAAACTCAGCTTTACTCAACGCCTCTTGTGCAG
AF222820/-        AATGAAGGGAGTGTATATTAACACAGCGTTGCTCAATGCATCTTGTGCAG

NC_002022/-       CAATGGATGATTTCCAATTAATTCCAATGATAAGCAAGTGTAGAACTAAG
X17336/-          CAATGGATGATTTCCAATTAATTCCAATGATAAGCAAGTGTAGAACTAAG
M21850/-          CTATGGATGACTTCCAGCTGATCCCAATGATAAGCAAATGCAGGACCAAA
AF156457/-        CTATGGATGACTTTCAACTGATTCCAATGATCAGCAAGTGTAGAACTAAA
M26087/-          CGATGGATGACTTCCAATTAATCCCGATGATAAGCAAATGCAGGACCAAG
M26088/-          CCATGGATGATTTTCAGTTGATCCCAATGATAAGCAAATGCAGAACCAAA
AF222820/-        CCATGGATGACTTCCAATTGATTCCAATGATAAGCAAATGCAGAACAAAA

NC_002022/-       GAGGGAAGGCGAAAGACCAACTTGTATGGTTTCATCATAAAAGGAAGATC
X17336/-          GAGGGAAGGCGAAAGACCAATTTGTACGGTTTCATCATAAAAGGAAGATC
M21850/-          GAAGGAAGACGGAAGACGAATCTGTATGGATTCATTATAAAAGGAAGATC
AF156457/-        GAGGGAAGAAGAAAGACAAATTTGTATGGGTTCATTATAAAAGGGAGATC
M26087/-          GAAGGGAGAAGGAAGACAAATTTGTATGGATTCATCATAAAGGGAAGGTC
M26088/-          GAAGGACGACGGAAAACAAATTTGTATGGATTCATCATAAAGGGAAGGTC
AF222820/-        GAAGGGAGACGGAAAACAAACCTGTATGGGTTCATTATCAAGGGAAGGTC

NC_002022/-       CCACTTAAGGAATGACACCGACGTGGTAAACTTTGTGAGCATGGAGTTTT
X17336/-          CCACTTAAGGAATGACACCGATGTGGTAAACTTTGTGAGCATGGAGTTTT
M21850/-          TCACTTGAGGAATGATACTGATGTGGTGAATTTTGTGAGCATGGAGTTCT
AF156457/-        CCACCTGAGGAACGACACCGATGTGGTAAACTTTGTGAGCATGGAGTTTT
M26087/-          CCATTTAAGAAATGACACTGACGTGGTAAACTTTGTAAGCATGGAGTTTT
M26088/-          TCATTTGAGGAATGATACTGATGTGGTGAATTTTGTGAGCATGGAATTTT
AF222820/-        CCATTTGAGGAATGATACTGATGTGGTAAACTTTGTGAGCATGGAATTTT
```

FIG. 10F

```
NC_002022/-     CTCTCACTGACCCAAGACTTGAACCACACAAATGGGAGAAGTACTGTGTT
X17336/-        CCCTCACTGACCCAAGACTTGAACCACACAAATGGGAGAAGTACTGTGTT
M21850/-        CTCTCACTGACCCGAGGCTTGAGCCACACAAGTGGGAGAAGTATTGTGTT
AF156457/-      CCCTCACTGACCCGAGGCTTGAACCGCACAAATGGGAGAAGTACTGTGTT
M26087/-        CTCTCACCGATCCAAGACTTGAGCCACACAATTGGGAGAAGTACTGTGTT
M26088/-        CTCTTACTGACCCTAGATTAGAACCACACAAGTGGGAGAAGTATTGTGTC
AF222820/-      CTCTTACAGACCCGAAACTGGAACCACACAAGTGGGAGAAGTACTGTGTT

NC_002022/-     CTTGAGATAGGAGATATGCTTCTAAGAAGTGCCATAGGCCAGGTTTCAAG
X17336/-        CTTGAGGTAGGAGATATGCTTCTAAGAAGTGCCATAGGCCATGTGTCAAG
M21850/-        CTTGAAATAGGAGACATGCTCCTGCGGACTGCAATAGGCCAAGTATCAAG
AF156457/-      CTTGAAATAGGGGACATGCTTCTAAGAACTGCCATAGGCCAAGTTTCGAG
M26087/-        CTAGAAATCGGAGACATGCTCCTAAGAACTGCTGTAGGCCAAGTGTCAAG
M26088/-        CTTGAAATAGGGGATATGCTCCTACGAACTGCAATAGGCCAAGTTTCAAG
AF222820/-      CTTGAAGTAGGGGACATGCTCCTGAGAACTTCAATAGGCCAGGTGTCAAG

NC_002022/-     GCCCATGTTCTTGTATGTGAGGACAAATGGAACCTCAAAAATTAAAATGA
X17336/-        GCCTATGTTCTTGTATGTGAGGACAAATGGAACCTCAAAAATTAAAATGA
M21850/-        GCCCATGTTCCTGTATGTGAGAACCAATGGAACCTCCAAAATCAAGATGA
AF156457/-      GCCCATGTTCCTGTATGTGAGAACGAATGGGACCTCCAAAATCAAAATGA
M26087/-        ACCCATGTTTTTGTATGTAAGGACCAATGGGACCTCTAAAATTAAAATGA
M26088/-        ACCCATGTTTCTGTATGTGACAACCAATGGAACTTCCAAGATCAAAATGA
AF222820/-      GCCCATGTTCCTATACGTGAGAACCAATGGAACCTCCAAAATTAAAATGA

NC_002022/-     AATGGGGAATGGAGATGAGGCGTTGTCTCCTCCAGTCACTTCAACAAATT
X17336/-        AATGGGGGATGGAAATGAGGCGTTGCCTCCTTCAGTCACTTCAACAAATC
M21850/-        AATGGGGTATGGAGATGAGACGTTGCCTTCTTCAGTCCCTTCAACAGGTT
AF156457/-      AATGGGGGATGGAAATGAGACGCTGTCTTCTCCAGTCCCTTCAACAAATT
M26087/-        AATGGGGAATGGAAATGAGGCGCTGCCTCCTTCAGTCTCTACAGCAGATT
M26088/-        AATGGGGTATGGAGATGAGGCGTTGTCTTCTTCAATCCCTCCAGCAAATC
AF222820/-      AATGGGGAATGGAGATGAGGCGTTGCCTCCTTCAATCCCTTCAACAAATT

NC_002022/-     GAGAGTATGATTGAAGCTGAGTCCTCTGTCAAAGAGAAAGACATGACCAA
X17336/-        GAGAGTATGATTGAAGCTGAGTCCTCTGTCAAGGAGAAAGACATGACCAA
M21850/-        GAAAGCATGGTTGAGGCTGAGTCCTCTGTCAAGGAGAAAGACATGACTAA
AF156457/-      GAGAGTATGATTGAAGCCGAGTCCTCTGTCAAAGAGAAGGACATGACCAA
M26087/-        GAAAGCATGACTGAAGCTGAGTCCTCAGTCAAAGAAAAGGACATGACCAA
M26088/-        GAAAGCATGATTGAGGCCGAGTCCTCTGTCAAGGAAAAAGACATGACTAA
AF222820/-      GAGAGCATGATTGAGGCAGAGTCTTCTATCAAAGAGAAGGACATGACCAA

NC_002022/-     AGAGTTCTTTGAGAACAAATCAGAAACATGGCCCATTGGAGAGTCTCCCA
X17336/-        AGAGTTCTTTGAAAACAAATCAGAAACATGGCCCGTTGGAGAGTCCCCCA
M21850/-        GGAATTCTTTGAAAACAAGTCAAAGACGTGGCCCATTGGAGAATCACCTA
```

FIG. 10G

```
AF156457/-      AGAGTTCTTTGAAAACAAATCAGAAACATGGCCTATTGGGGAATCTCCCA
M26087/-        AGAATTCTTTGAGAACAAATCGGAGACATGGCCTATAGGAGAGTCCCCCA
M26088/-        AGAATTCTTTGAAAACAAGTCGGAGACATGGCCCATTGGAGAATCACCCA
AF222820/-      AGAATTTTTTGAAAACAAGTCGGAGACGTGGCCGATTGGAGAGTCACCTA

NC_002022/-     AAGGAGTGGAGGAAAGTTCCATTGGGAAGGTCTGCAGGACTTTATTAGCA
X17336/-        AAGGAGTGGAGGAAGGTTCCATTGGGAAGGTCTGCAGAACTTTATTGGCA
M21850/-        AAGGAGTGGAAGAAGGTTCCATCGGGAAAGTGTGCAGGACCTTACTGGCG
AF156457/-      AGGGGGTGGAGGAAGGATCCATTGGAAAGGTCTGCAGGACTCTGTTGGCA
M26087/-        AAGGAGTGGAAGAAGGCTCAATCGGGAAAGTTTGCAGGACCTTGTTAGCA
M26088/-        AAGGAGTAGAAGAAGGTTCCATTGGGAAAGTATGCAGGACTCTGCTAGCA
AF222820/-      AGGGAGTGGAGGAAGGCTCCATCGGGAAGGTGTGCAGGACCTTACTAGCA

NC_002022/-     AAGTCGGTATTTAACAGCTTGTATGCATCTCCACAACTAGAAGGATTTTC
X17336/-        AAGTCGGTATTCAACAGCTTGTATGCATCTCCACAACTGGAAGGATTTTC
M21850/-        AAGTCTGTATTTAACAGCTTATATGCATCCCCACAACTTGAGGGATTTTC
AF156457/-      AAGTCTGTATTCAACAGCTTGTACGCATCTCCACAGCTGGAAGGTTTCTC
M26087/-        AAATCTGTGTTTAACAGTTTATATGCATCTCCACAACTCGAAGGGTTTTC
M26088/-        AAGTCTGTATTCAACAGCTTGTATGCATCTCCACAACTTGAAGGTTTTTC
AF222820/-      AAGTCTGTGTTCAACAGCTTGTATGCATCTCCACAACTCGAGGGGTTTTC

NC_002022/-     AGCTGAATCAAGAAAACTGCTTCTTATCGTTCAGGCTCTTAGGGACAATC
X17336/-        AGCTGAATCAAGAAAACTGCTTCTTATCGTTCAGGCTCTTAGGGACAACC
M21850/-        AGCGGAATCTAGAAAACTGCTCCTCATTGTTCAGGCTCTTAGAGACAACC
AF156457/-      AGCTGAATCAAGGAAACTGCTTCTTATCGTTCAGGCTCTTAGGGACAACC
M26087/-        AGCTGAATCTAGGAAAATACTTCTCATTGTTCAGGCCCTTAGGGACAACC
M26088/-        AGCTGAGTCAAGAAAGCTGCTTCTCATTGTTCAGGCACTTAGGGACAACC
AF222820/-      AGCTGAATCAAGAAAACTGTTACTCATTGTTCAGGCACTTAGGGACAACC

NC_002022/-     TGGAACCTGGGACCTTTGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
X17336/-        TGGAACCTGGGACCTTTGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
M21850/-        TGGAACCTGGAACCTTCGATCTTGGAGGGCTATATGGAGCAATTGAGGAG
AF156457/-      TGGAACCTGGAACCTTTGATCTTGGAGGATTGCATGAAGCAATTGAGGAG
M26087/-        TGGAACCTGGAACCTTTGATATTGGGGGGCTATATGAATCAATTGAGGAG
M26088/-        TGGAACCTGGCACCTTCGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
AF222820/-      TGGAACCTGGAACCTTCGACATTGAAGGACTGTATGAAGCAATTGAGGAG

NC_002022/-     TGCCTAATTAATGATCCCTGGGTTTTGCTTAATGCTTCTTGGTTCAACTC
X17336/-        TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCTTCTTGGTTCAACTC
M21850/-        TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC
AF156457/-      TGCCTGATTAATGACCCCTGGGTTTTGCTTAATGCATCTTGGTTTAACTC
M26087/-        TGTCTGATTAATGATCCCTGGGTTTTGCTCAATGCATCTTGGTTCAACTC
M26088/-        TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC
AF222820/-      TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC
```

FIG. 10H

```
NC_002022/-          GTTCCTTACACATGCATTGAGTTAGTTGTGGCAGTGCTACTATTTGCTAT
X17336/-             CTTCCTCACACATGCATTGAGATAGTTGTGGCAATGCTACTATTTGCTAT
M21850/-             CTTCCTCACACATGCACTGAAATAGTTGTGGCAATGCTACTATTTGCTAT
AF156457/-           CTTCCTCACACATG-----------------------------------
M26087/-             CTTCCTTACACATGCACTAAAGTAGTTGTGGCAATGCTACTATTTGCTAT
M26088/-             CTTCCTCACACATGCACTGAAATAGTTGTGGCAATGCTACTATTTGCTAT
AF222820/-           C-------------------------------------------------

NC_002022/-          CCATACTGTCCAAAAAAGTACCTTGTTTCTACT-- (SEQ ID NO: 127)

X17336/-             CCATACTGTCCAAAAAAGTACCTTGTTTCTACT-- (SEQ ID NO: 128)

M21850/-             CCATACTGTCCAAAAAAGTACCTTGTTTCTACT-- (SEQ ID NO: 129)

AF156457/-           ---------------------------------- (SEQ ID NO: 130)

M26087/-             CCATACTGTCCAAAAAAGTACCTTGTTTCTACT-- (SEQ ID NO: 131)

M26088/-             ACATCCTGTCCAAAAAAGTACCTTGTTTCTACT-- (SEQ ID NO: 132)

AF222820/-           ---------------------------------- (SEQ ID NO: 133)
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FIG. 10I

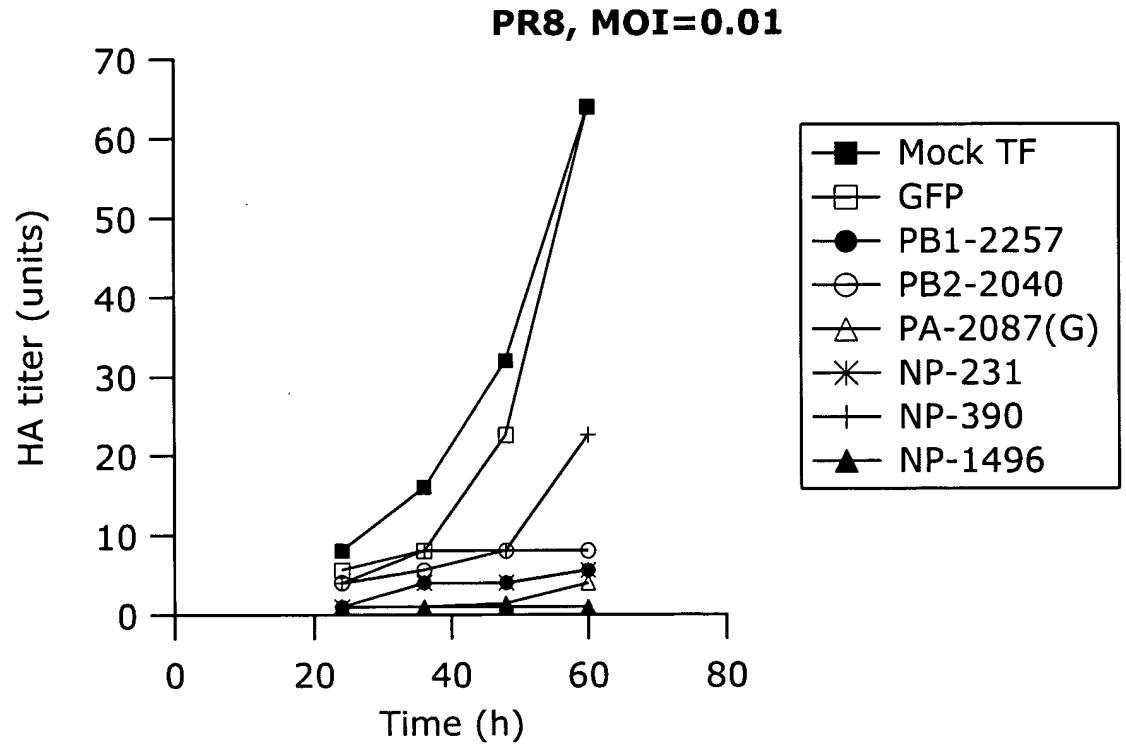


FIG. 11A

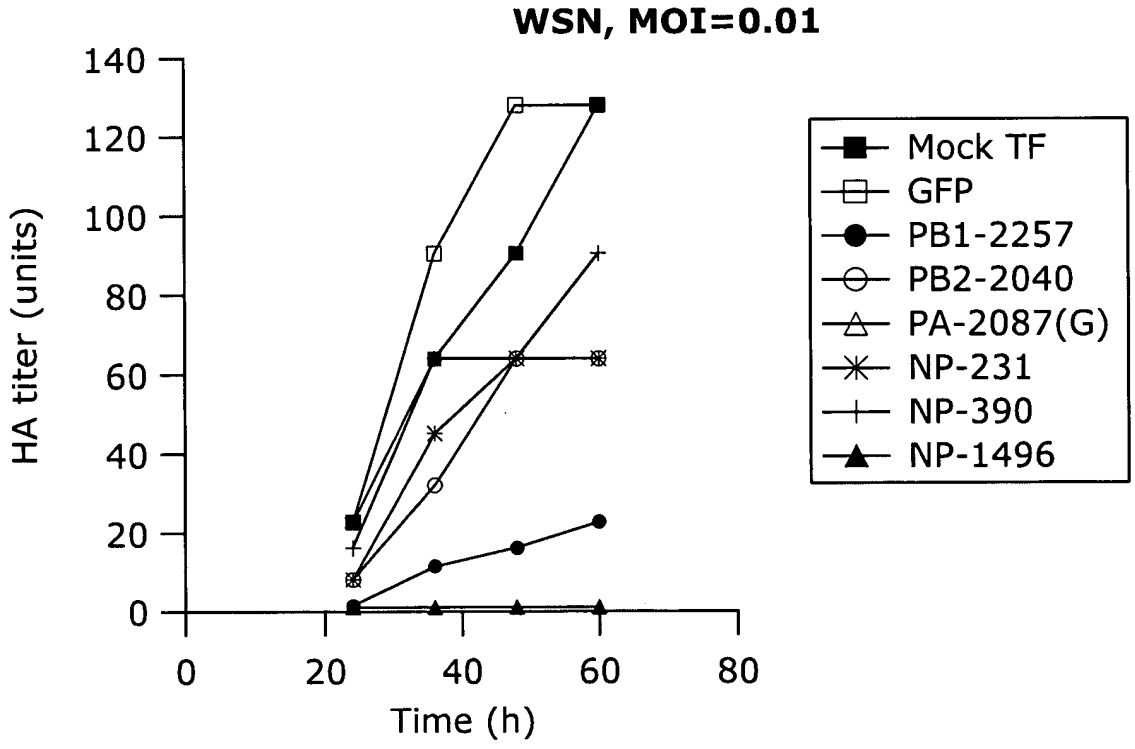
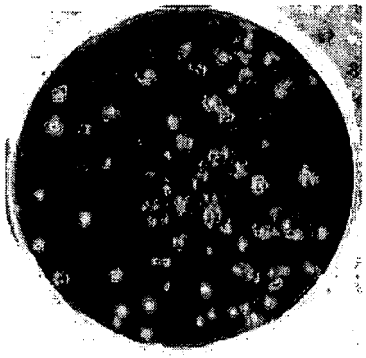
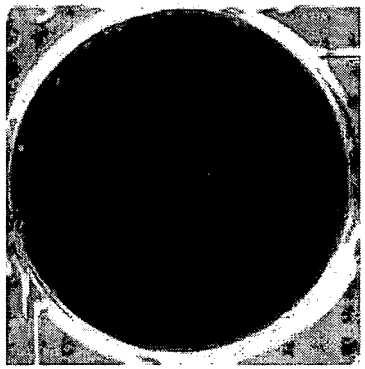


FIG. 11B

Potent inhibition of influenza A viral replication by NP-1496





	Mock transfection	NP-1496 siRNA 2.5 nmole	Fold difference
MOI=0.001	$6x10^5$ PFU/ml	<20 PFU/ml	$3x10^4$
MOI=0.1	$1x10^6$ PFU/ml	$5x10^3$ PFU/ml	$2x10^2$

FIG. 11C

BEST AVAILABLE COPY

BEST AVAILABLE COPY

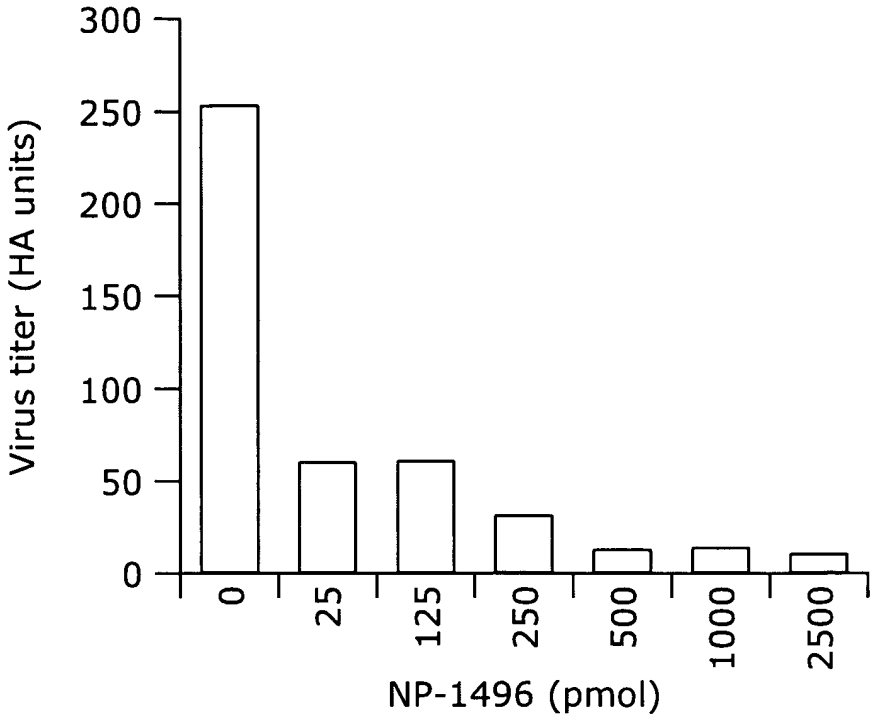


FIG. 11D

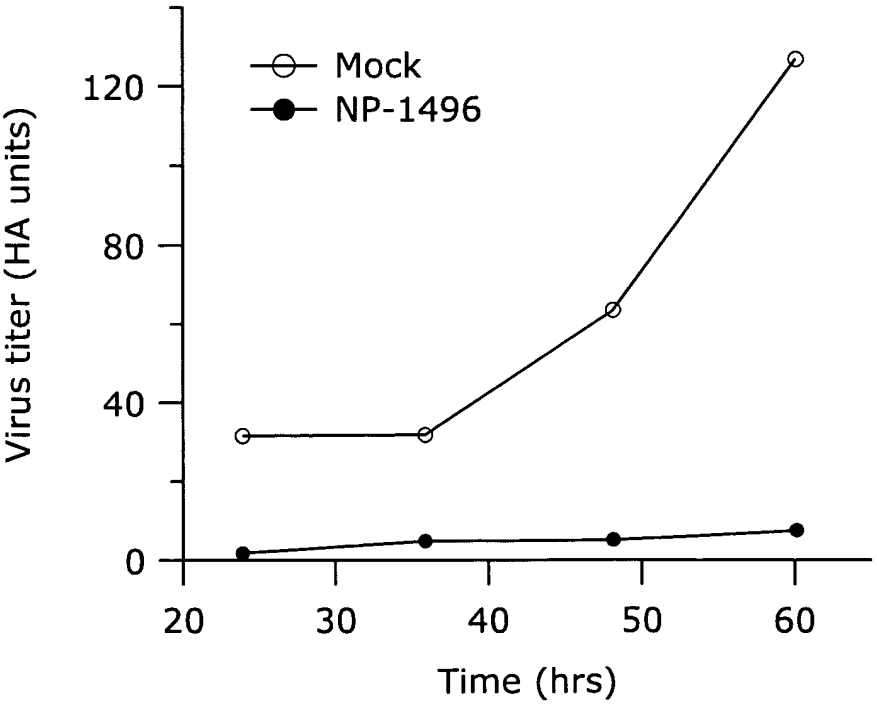


FIG. 11E

PR8 (H1N1)	TCTCGGACGAAAAGGCAGCGAGCCCGATCGTGCCTTCCTTTGACATGAGT	
WSN (H1N1)	TCTCGGACGAAAAGGCAGCGAGCCCGATCGTGCC**C**TCCTTTGACATGAGT	
Lenn.(H2N2)	TCTCGGAC**T**AAAAGGCA**A**CGA**A**CCC**C**ATCGTGCC**C**TC**T**TTTGACATGAGT	
HK (H3N2)	TCTCGGACGAAAAGGCAGCGA**A**CCCGATCGTGCC**C**TC**T**TTTGACATGAGT	
Memphis (H3N2)	TCTC**A**GACGAAAAGGCA**A**CGA**A**CCCGATCGTGCC**C**TC**T**TTTGACATGAGT	
HK (H5N1)	TCTC**A**GACGAAAAGGCA**A**CGA**A**CCCGATCGTGCCTTCCTTTGACATGAGT	
Duck (H10N7)	TCTCGGACGAAAAGGC**G**ACGAACCCGATCGTGCCTTCCTTTGACATGAGT	
Equine (H7N7)	TCTCGGACGAAAAGGCAACGAACCCGATCGTGCCTTCCTTTGACATGAGC	
Whale (H13N2)	TCTC**A**GACGAAAAGGCAACGAACCCGATCGTGCCTTCCTTTGACATGAGT	
Chicken (H9N2)	TCTCGGACGAAAAGGCAACGAACCCGATCGTGCCTTCCTTTGACATGAGT	
Swine (H4N6)	TCTCGGACGAAAAGGCAACGAACCCGATCGTGCCTTCCTTTGACATGAGT	

PR8 (H1N1)	AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGAGTACGACAATTA	(SEQ ID NO: 134)
WSN (H1N1)	AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGAGTACGACAATTA	(SEQ ID NO: 135)
Lenn.(H2N2)	AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGAGTACGACAATTA	(SEQ ID NO: 136)
HK (H3N2)	AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGAGTACGACAATTA	(SEQ ID NO: 137)
Memphis (H3N2)	AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGAGTACGACAATTA	(SEQ ID NO: 138)
HK (H5N1)	AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGA**A**TA**T**GACAATT**G**	(SEQ ID NO: 139)
Duck (H10N7)	AA**C**GA**G**GGATCTTATTTCTTCGGAGACAATGCAGAGGA**A**TA**T**GACAATTA	(SEQ ID NO: 140)
Equine (H7N7)	AATGAAGG**G**TCTTATTTCTTCGGAGACAATGC**T**GAGGAGT**TT**GACA**G**TTA	(SEQ ID NO: 141)
Whale (H13N2)	AATGA**G**GGATCTTATTTCTTCGGAGACAATGC**T**GAGGAGTA**T**GACAATT**G**	(SEQ ID NO: 142)
Chicken (H9N2)	AATGAAGGATCTTATTTCTTCGGAGACAATGCA**T**AGGAGTA**T**GACAATTA	(SEQ ID NO: 143)
Swine (H4N6)	AA**C**GAAGGGTCTTATTTCTTCGGAGACAATGCAGAGGA**A**TA**T**GACAATTA	(SEQ ID NO: 144)

FIG. 12

Summary of the inhibitory effect of siRNAs
on influenza A virus production

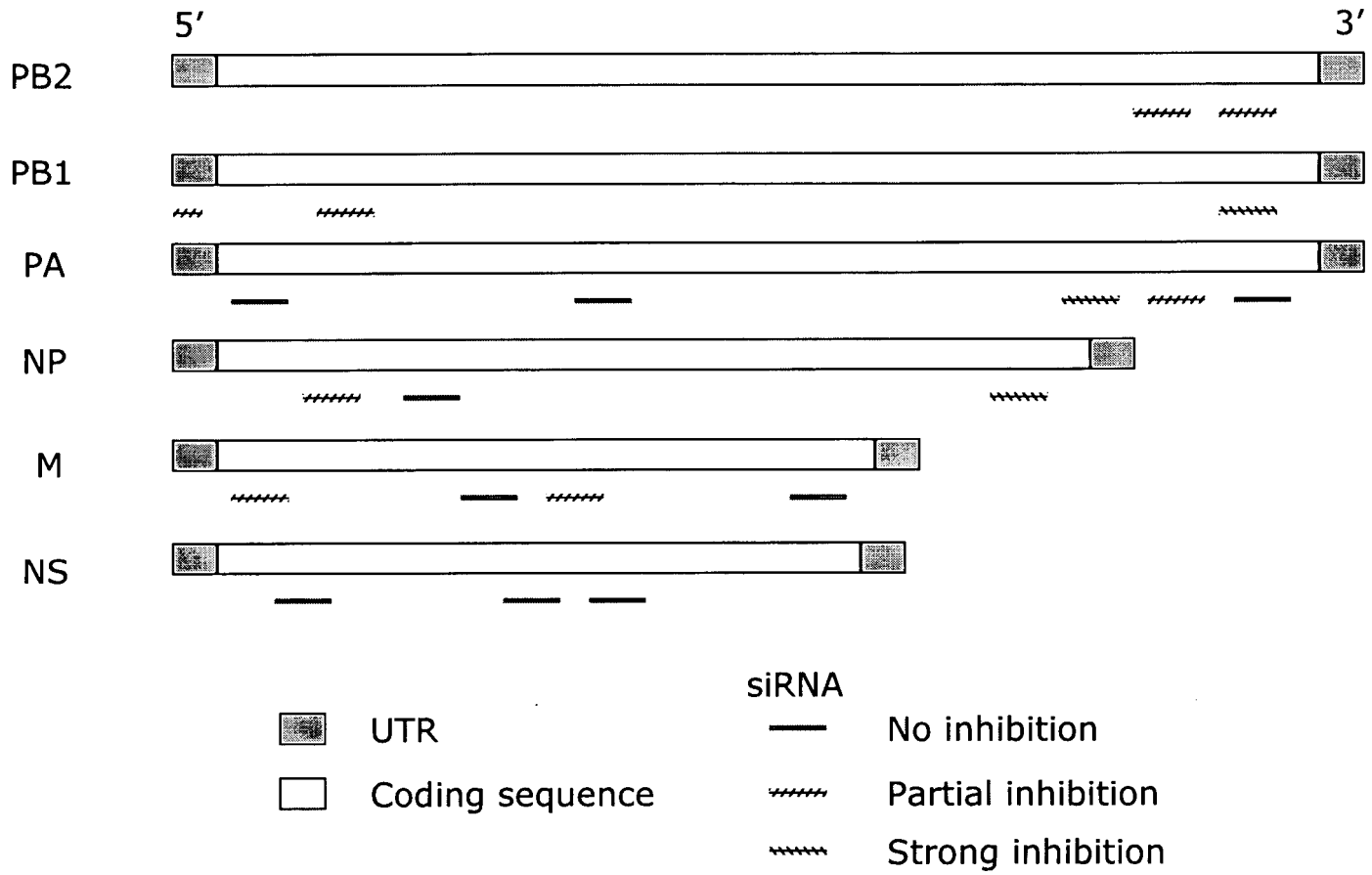


FIG. 13

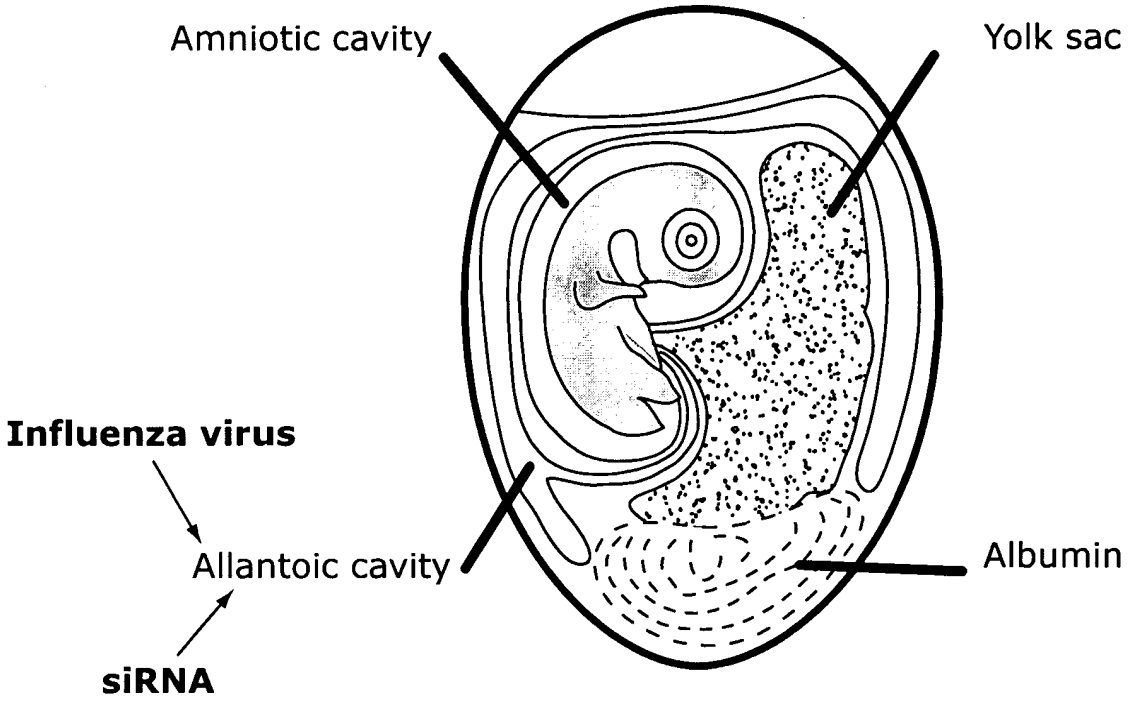


FIG. 14A

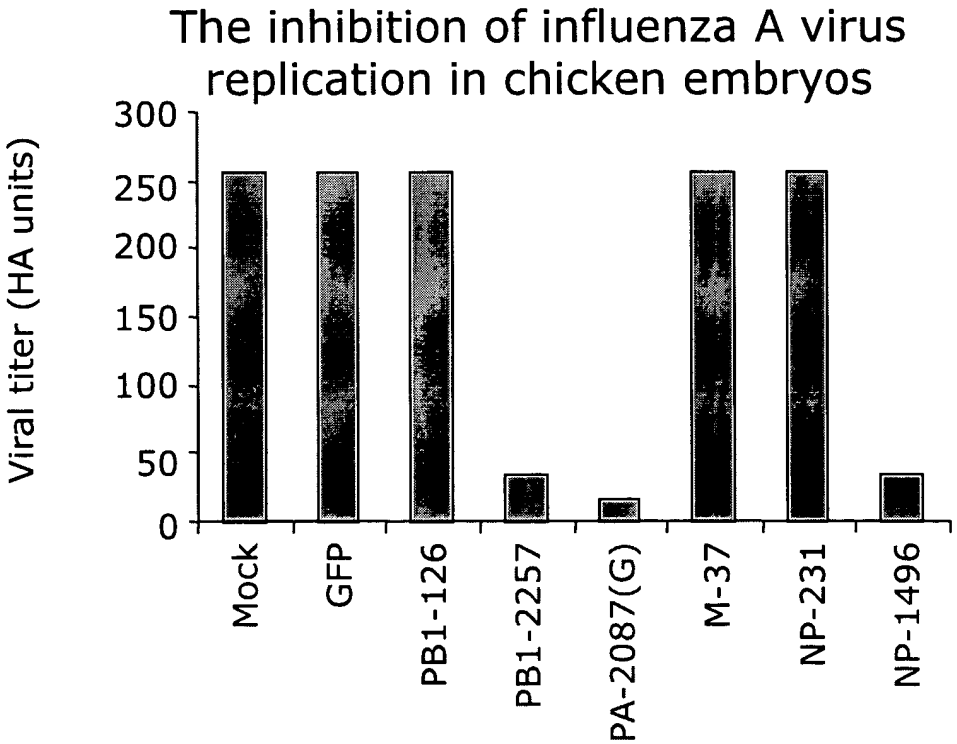


FIG. 14B

Nucleocapsid protein
RNA-binding protein pivotal to virus replication

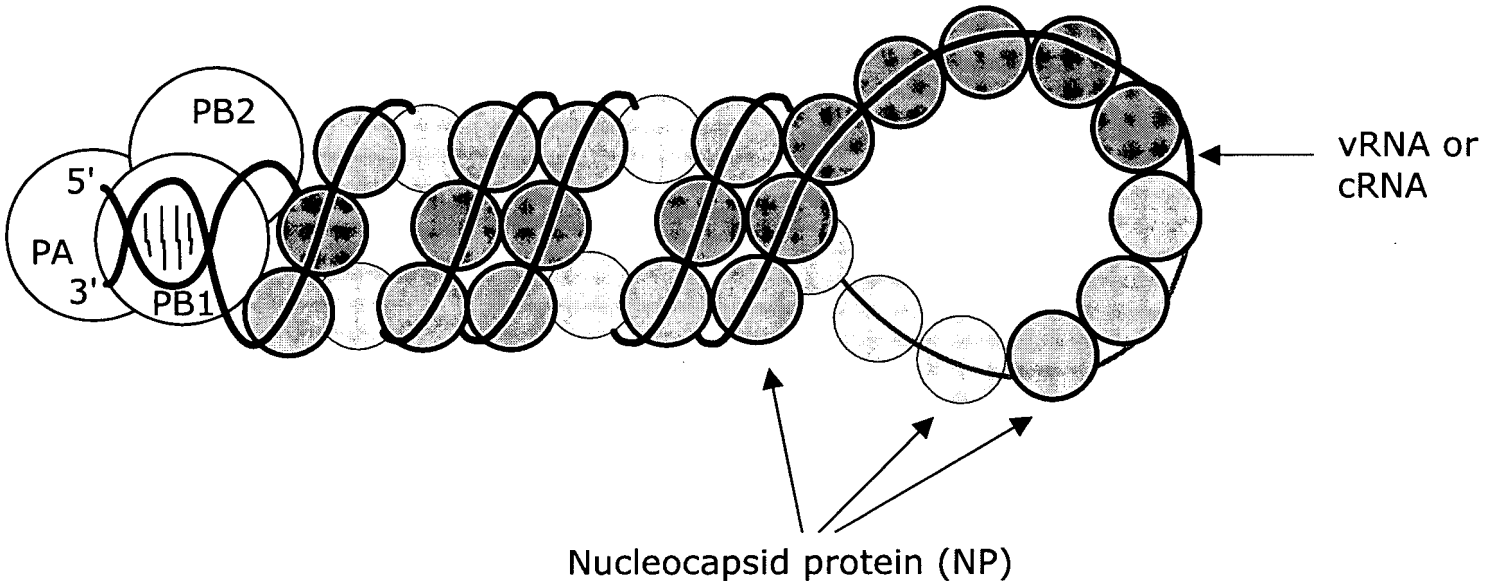


FIG. 15

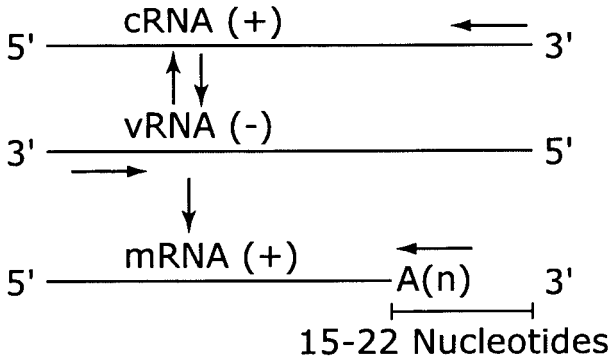


FIG. 16A

Diagram of Influenza Virus virion RNA (vRNA), mRNA and full-length cRNA or template RNA

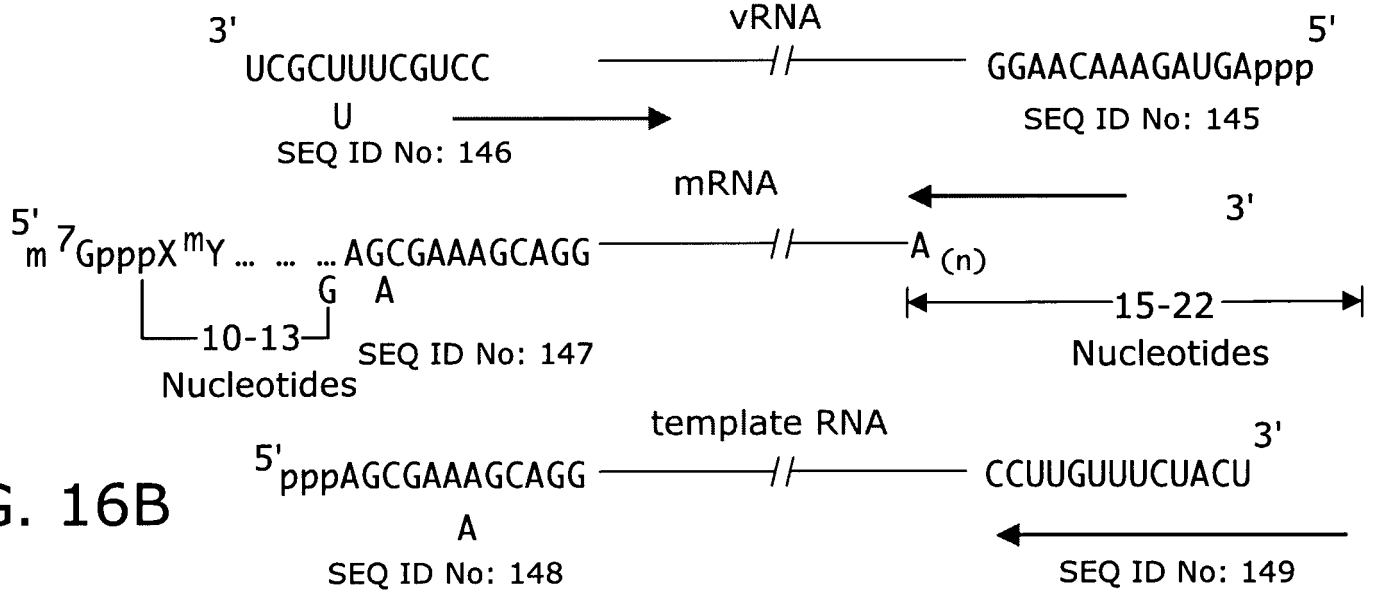


FIG. 16B

NP siRNA interferes with virus replication at a very early stage

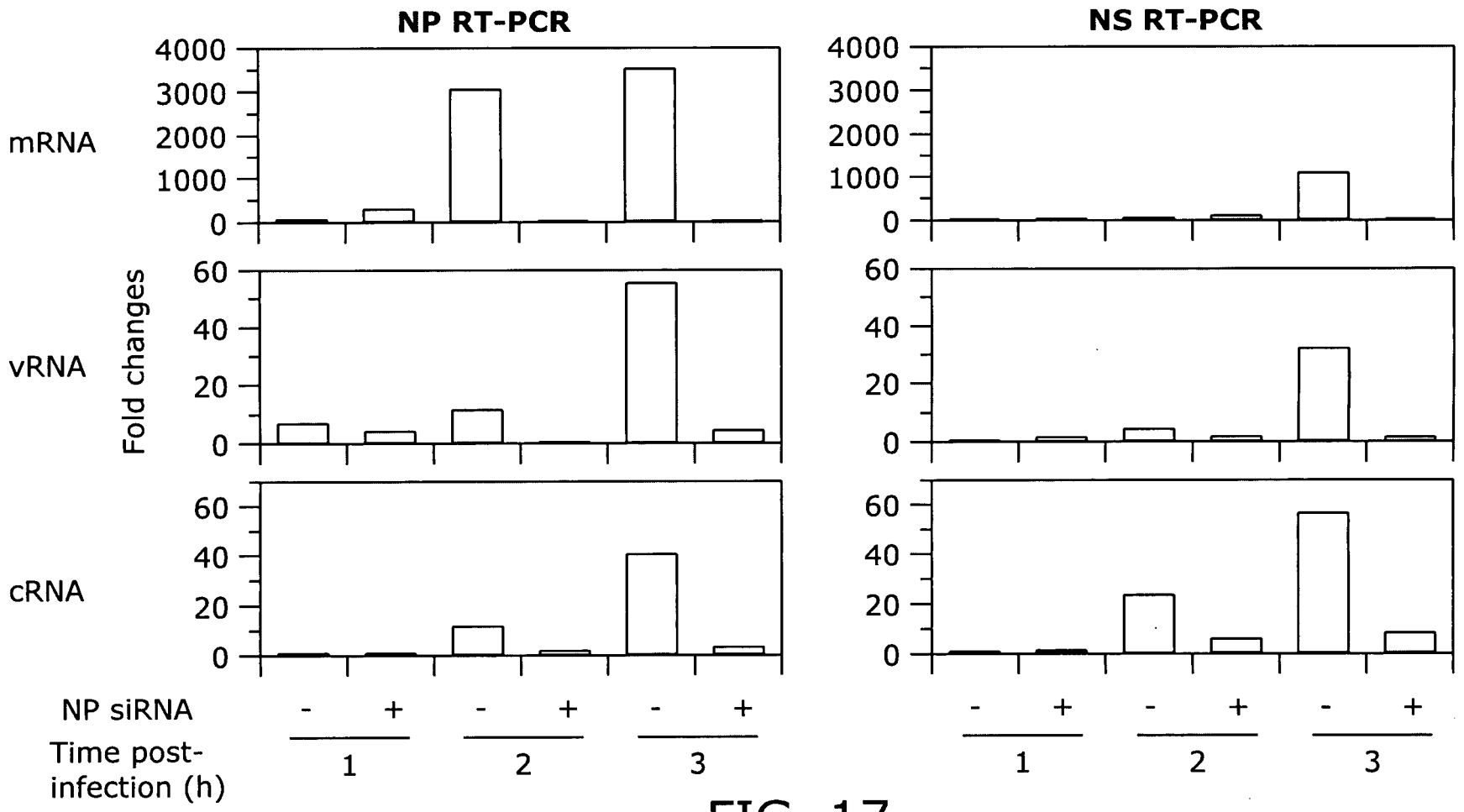


FIG. 17

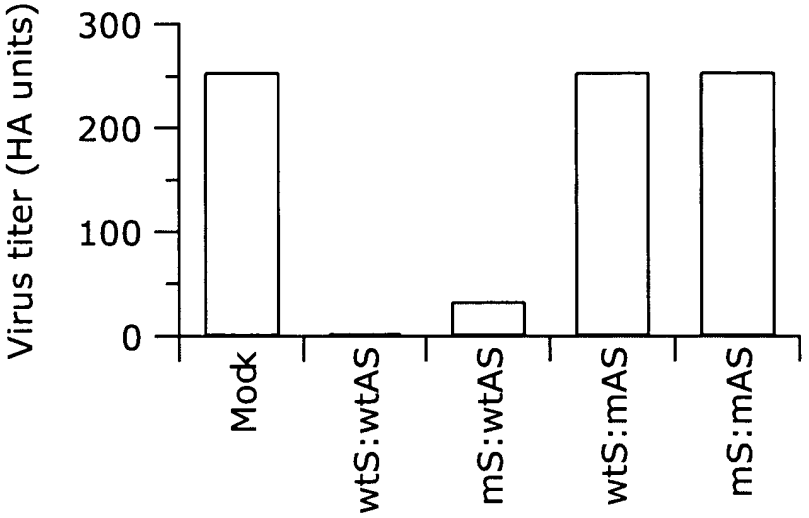


FIG. 18A

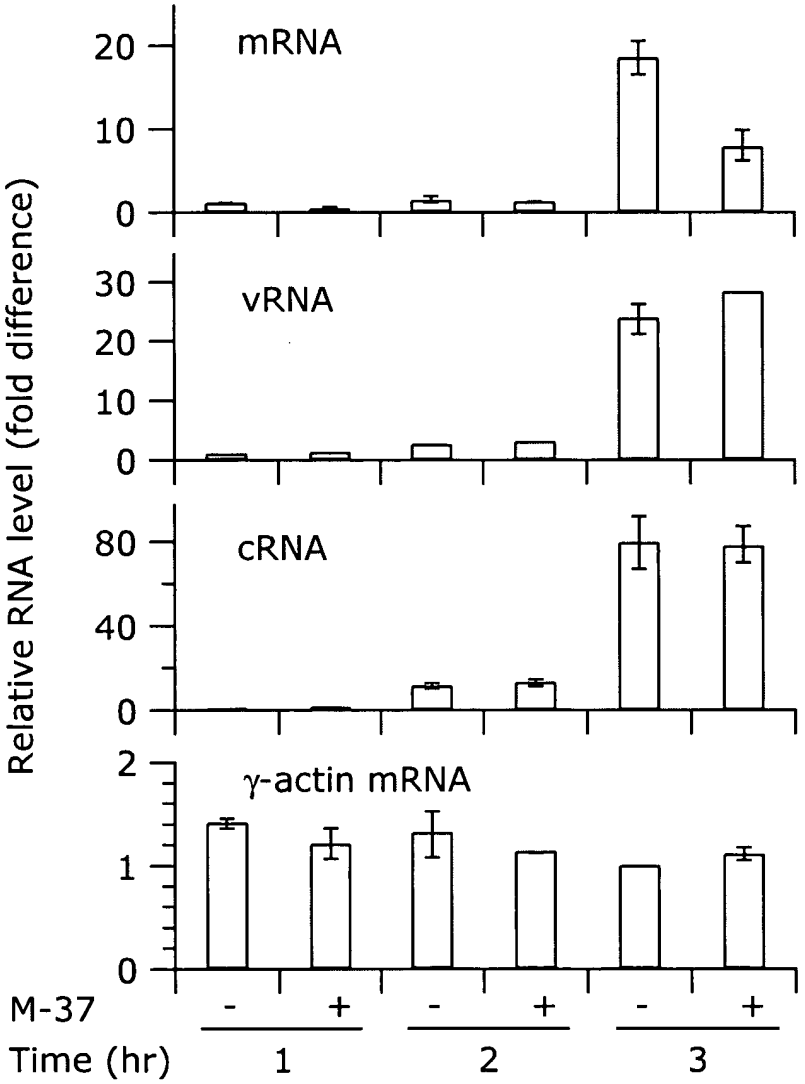


FIG. 18B

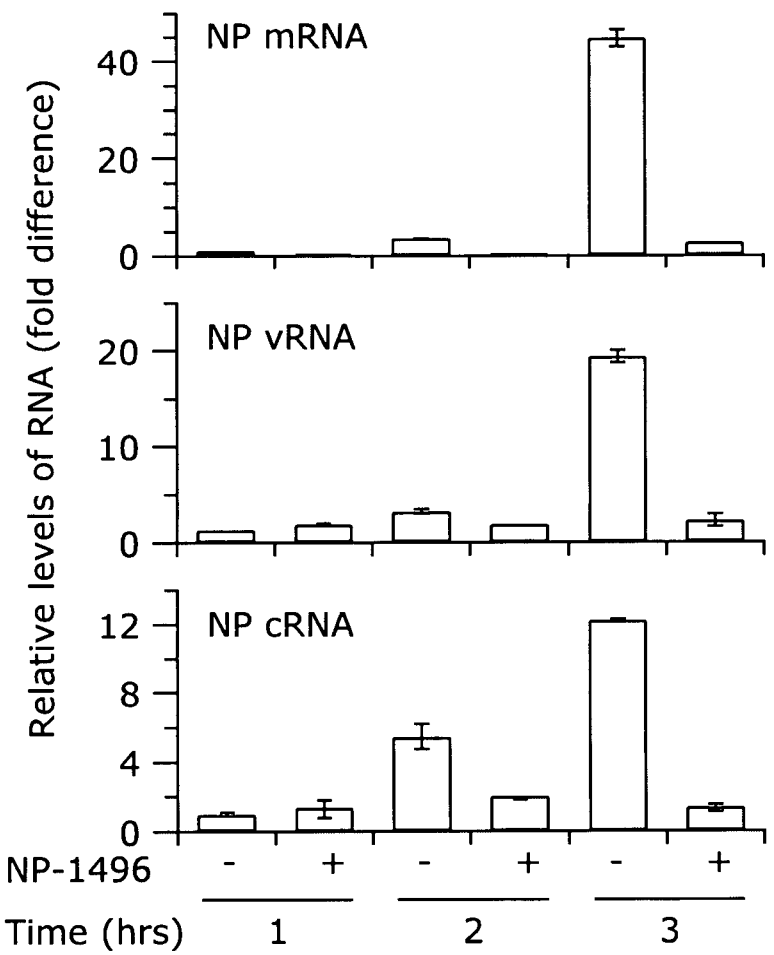


FIG. 19A

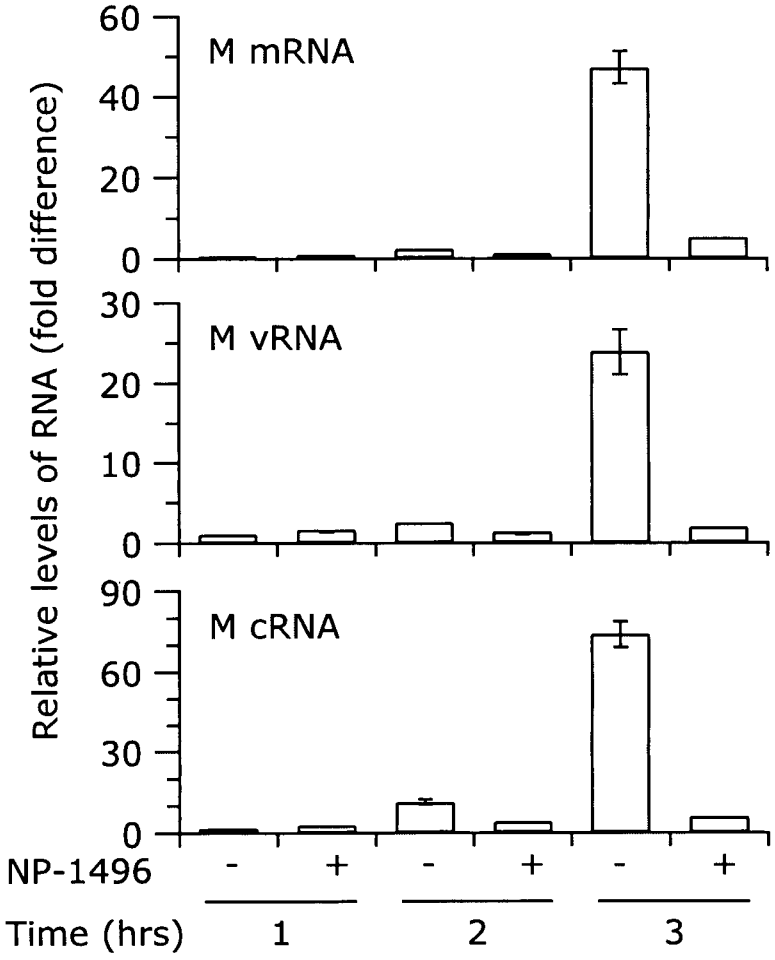


FIG. 19B

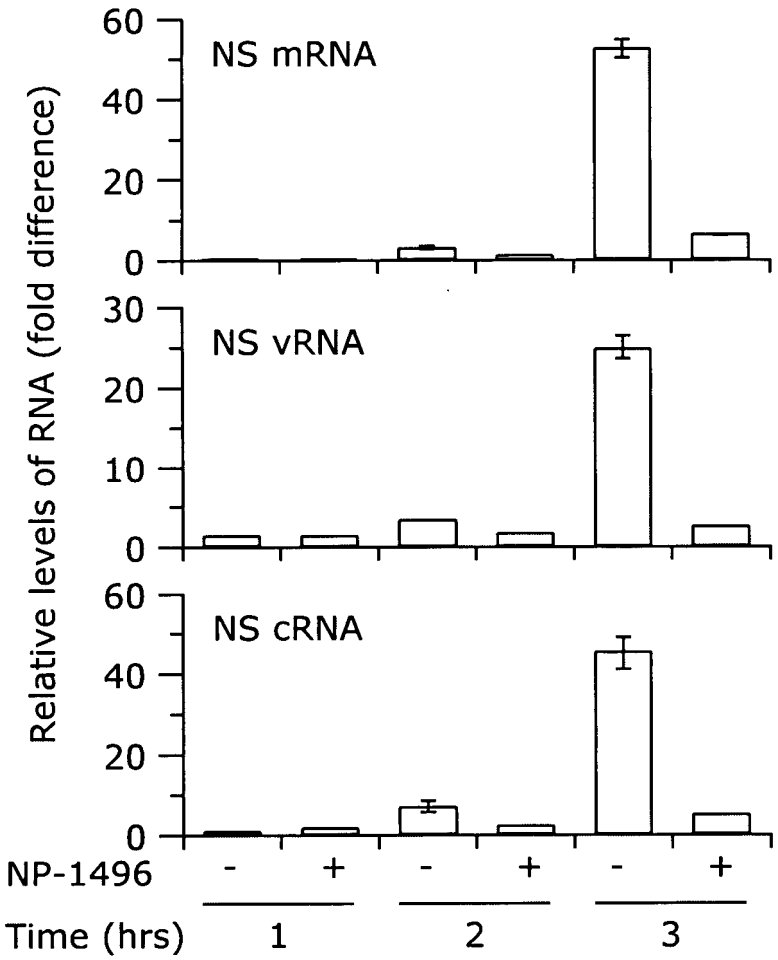


FIG. 19C

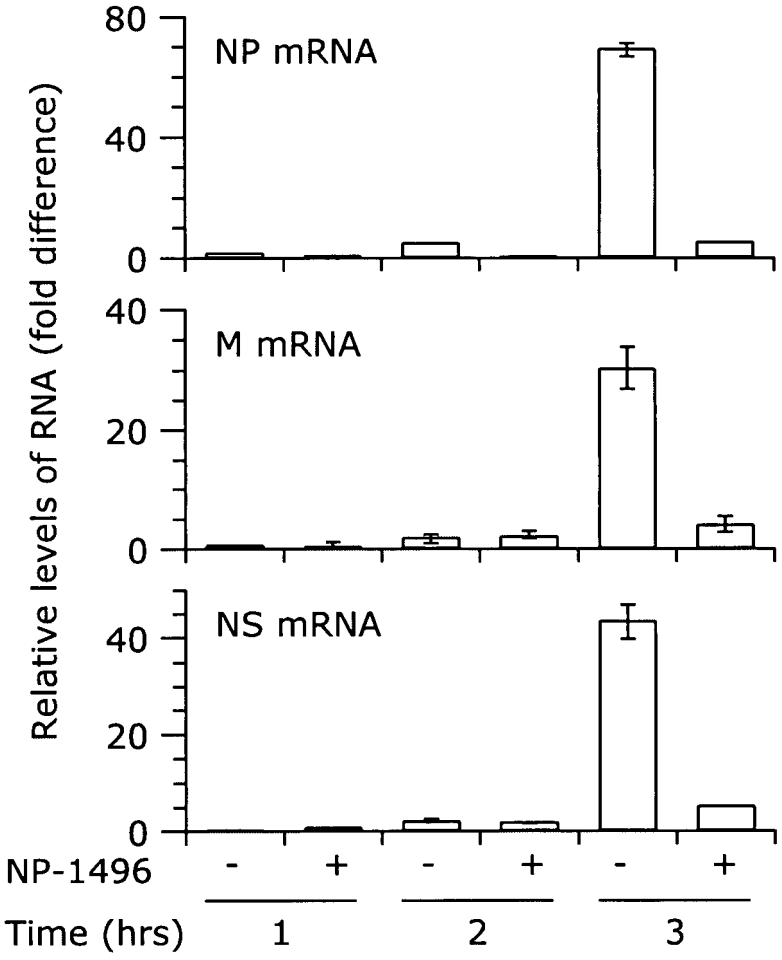


FIG. 19D

NP and PA siRNA interfere with viral mRNA transcription

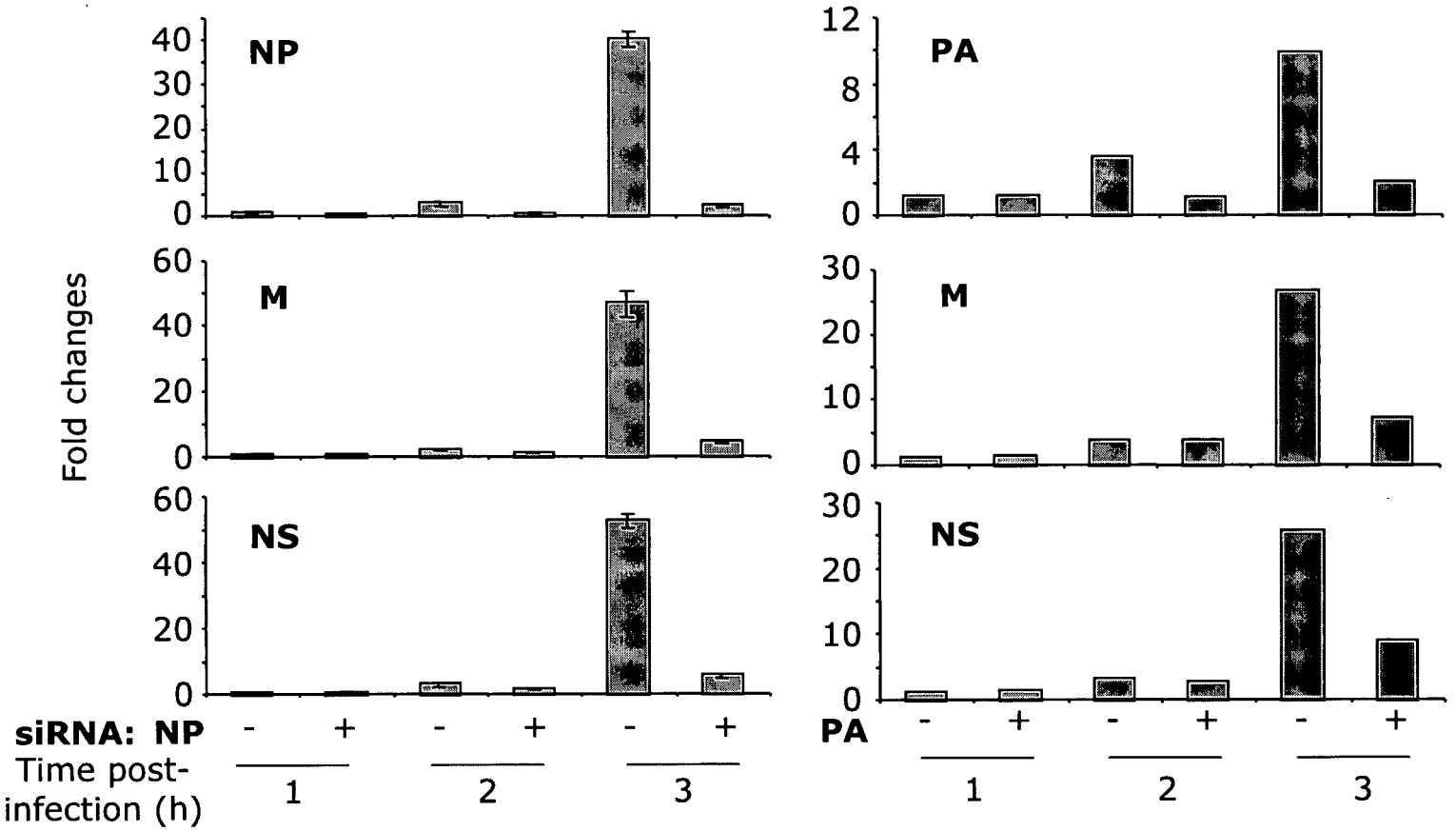


FIG. 19E

NP and PA siRNA interfere with viral vRNA replication

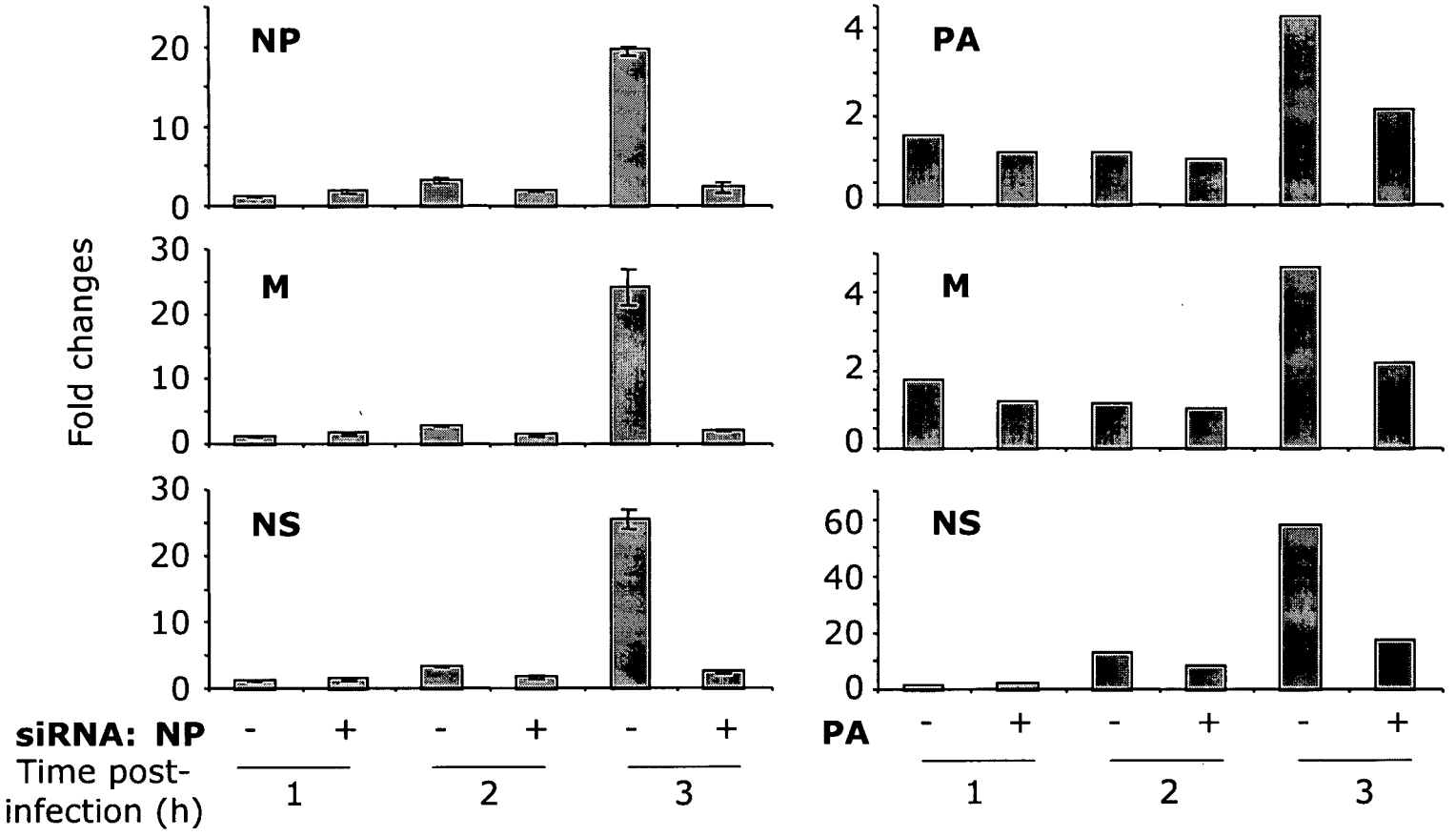


FIG. 19F

NP and PA siRNA interfere with viral cRNA replication

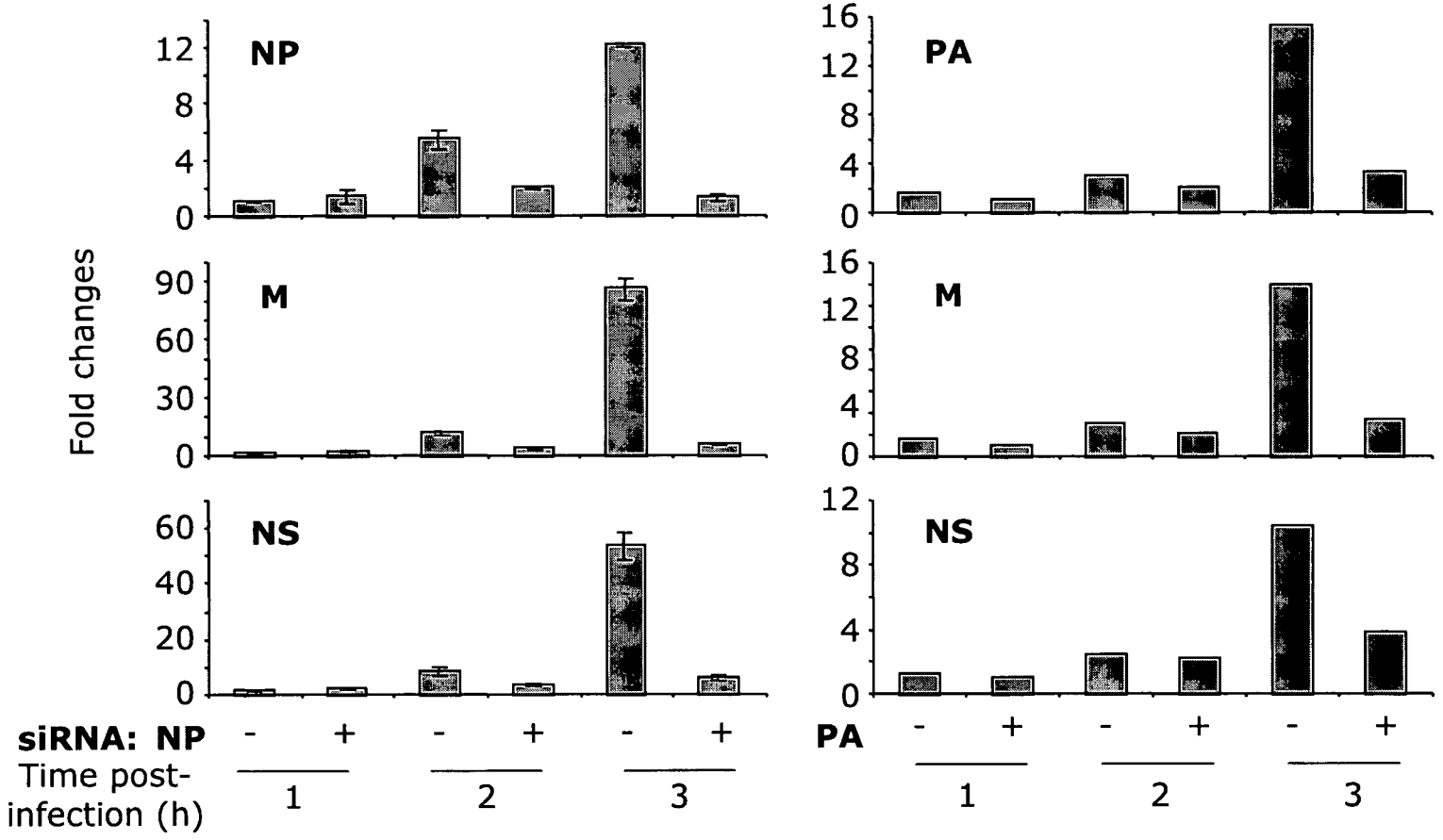


FIG. 19G

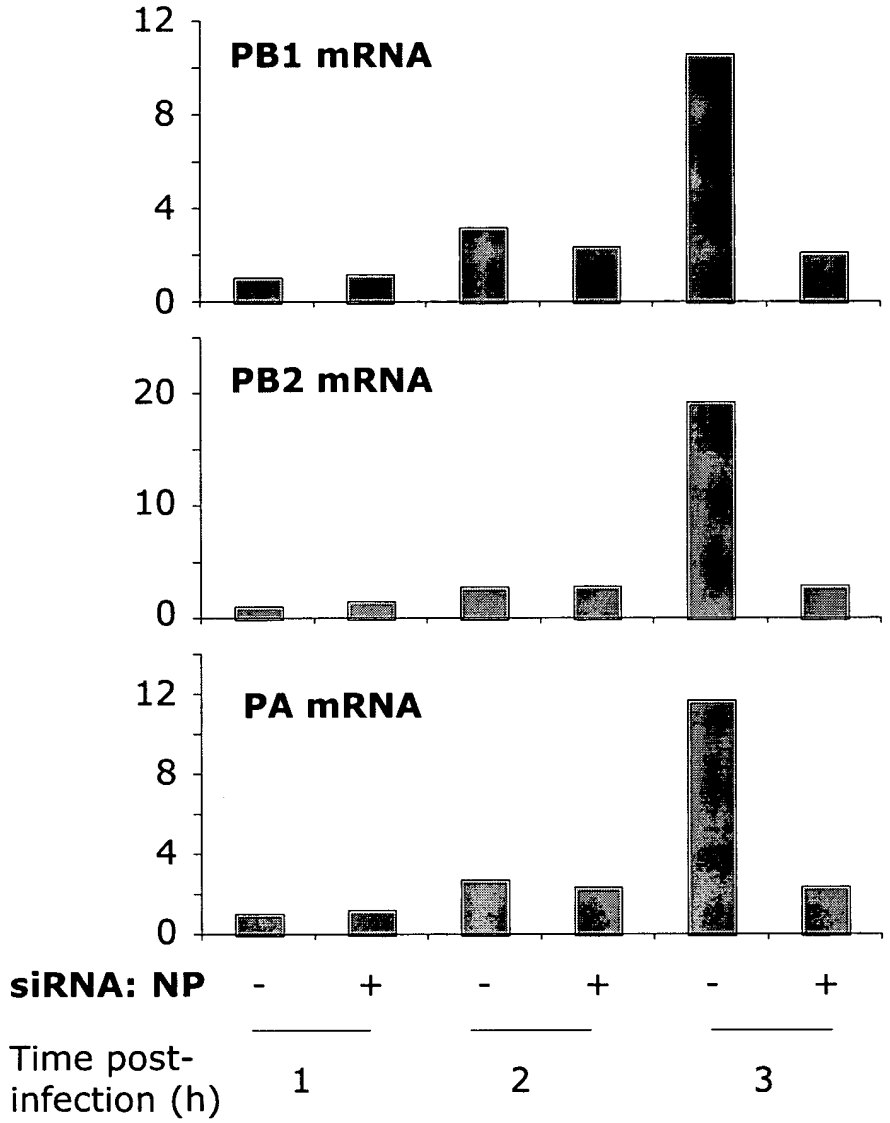

12
PB1 mRNA
8
4
0
20
PB2 mRNA
10
0
12
PA mRNA
8
4
0
siRNA: NP
-
+
-
+
-
+
Time post-infection (h)
1
2
3

FIG. 19H

SEQ ID No: 150

CD8-61

5'- gcuacaacuacuacaugacdtdt -3'
3'- dtdtcgauguugaugauguacug -5'

SEQ ID No: 151

CD8-61F

5'-cggggg u gcuacaacuacuacaugac g c a g
3'-gucccc uu cgauguugaugauguacug a c c g u

SEQ ID No: 152

FIG. 20A

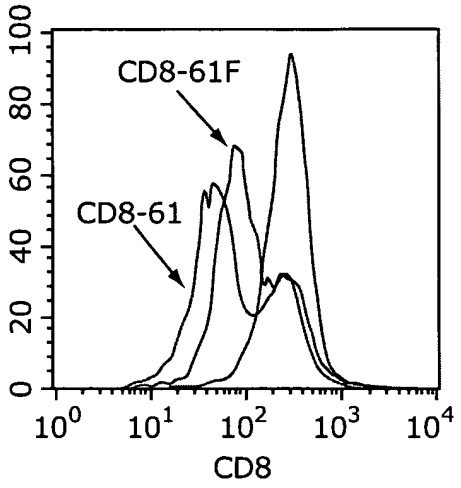


FIG. 20B

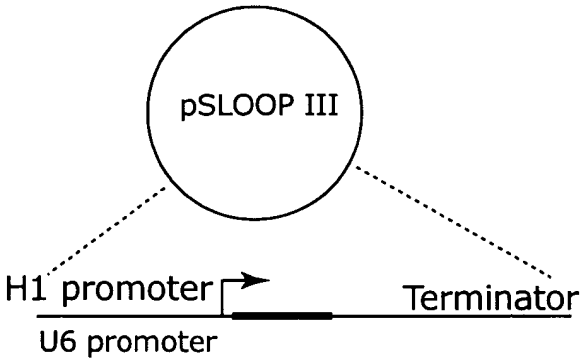


FIG. 20C

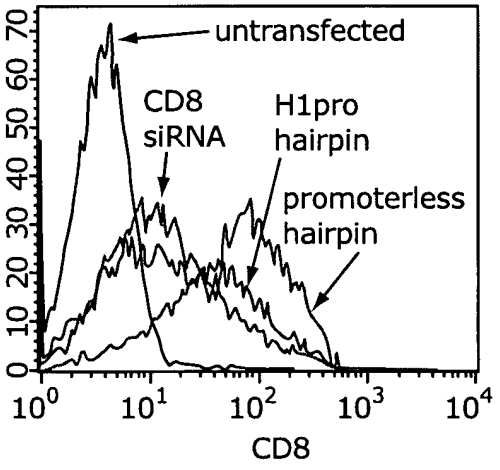


FIG. 20D

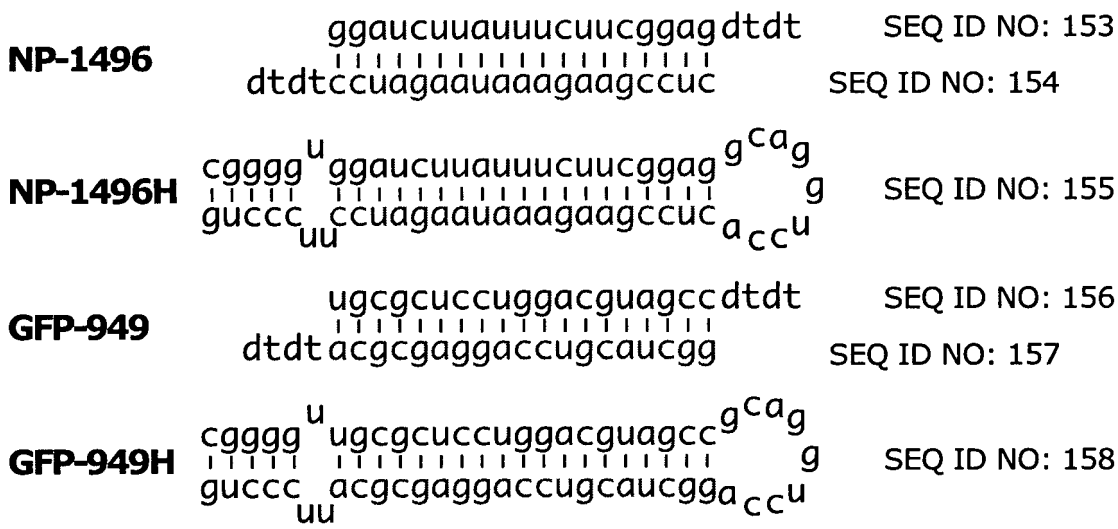


FIG. 21A

FIG. 21B

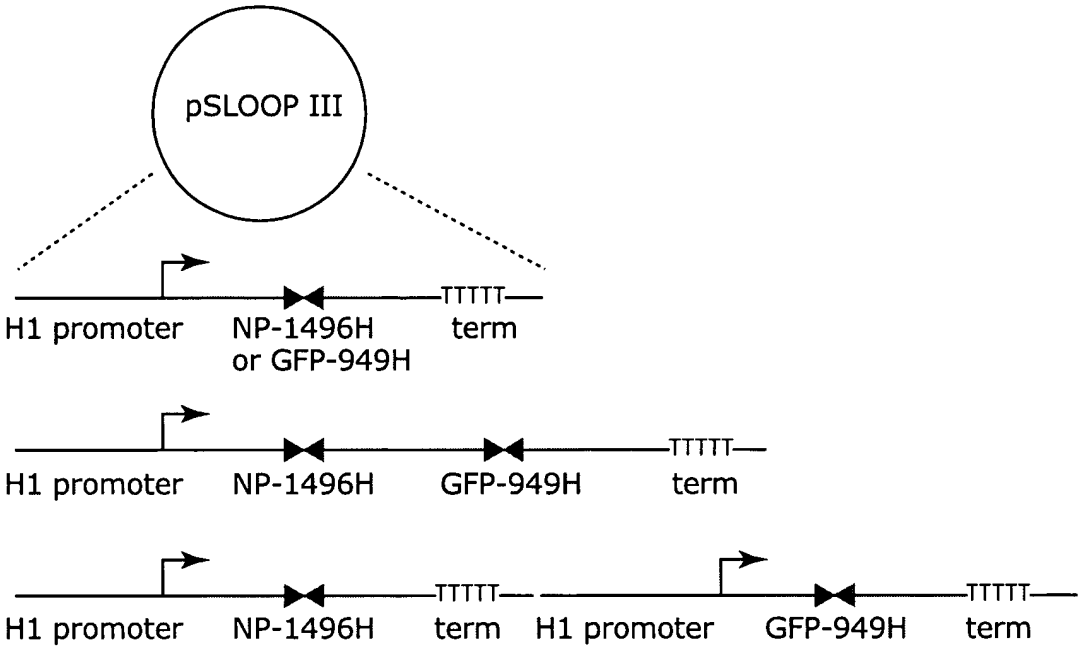

pSLOOP III
TTTTT
H1 promoter
NP-1496H
or GFP-949H
term
TTTTT
H1 promoter
NP-1496H
GFP-949H
term
TTTTT
TTTTT
H1 promoter
NP-1496H
term
H1 promoter
GFP-949H
term

FIG. 21C

siRNA prevents influenza virus production in mice

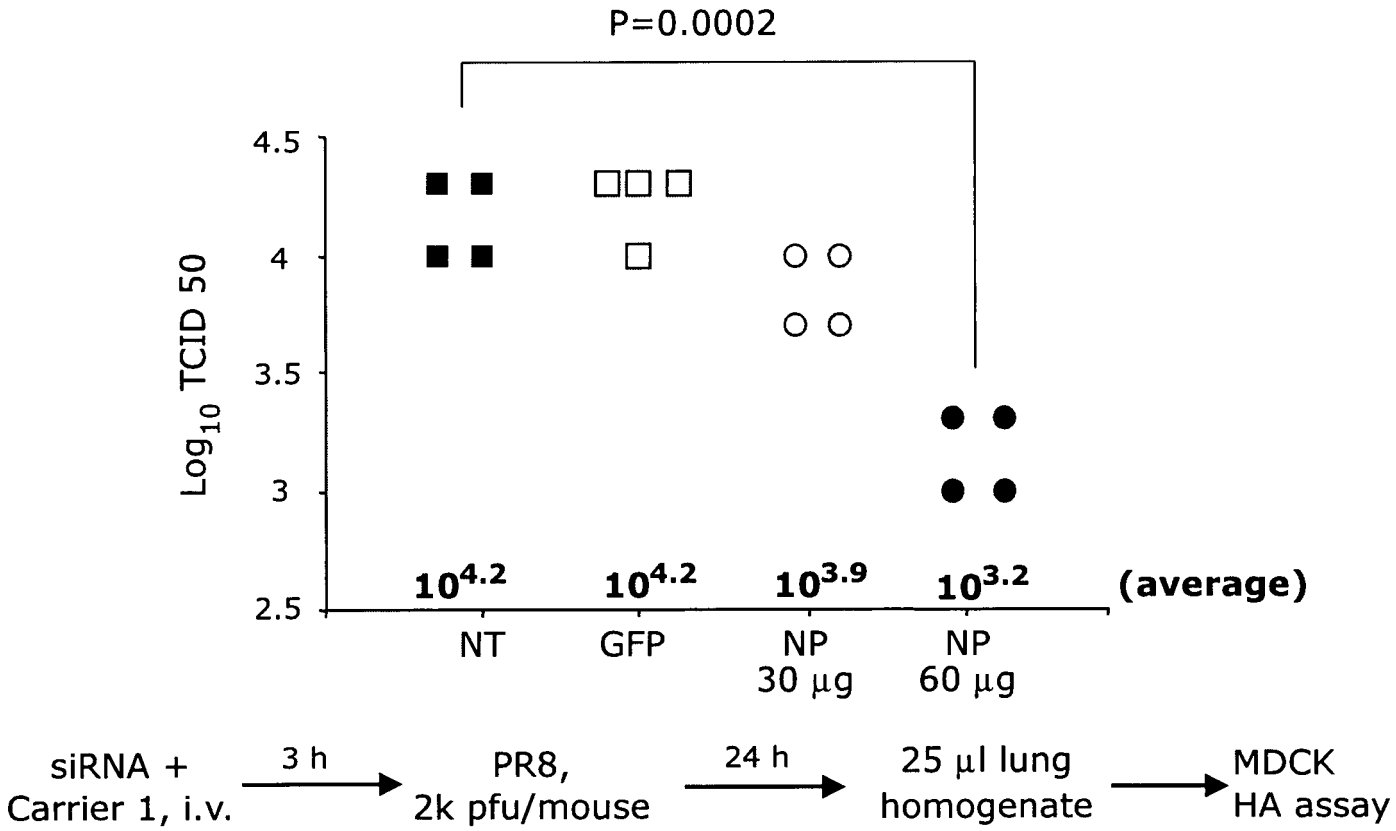


FIG. 22A

The in vivo transfection effect of Poly-L-Lysine (42k)

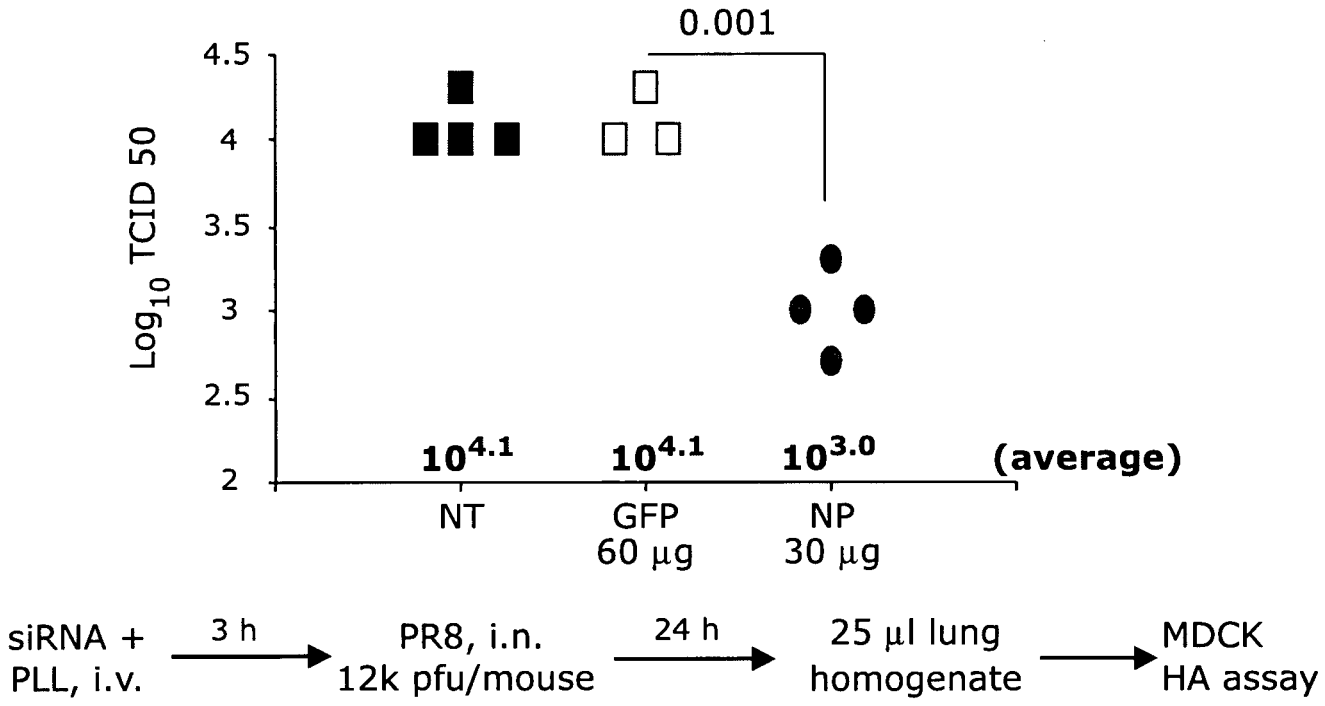


FIG. 22B

siRNA prevents influenza virus production in vivo

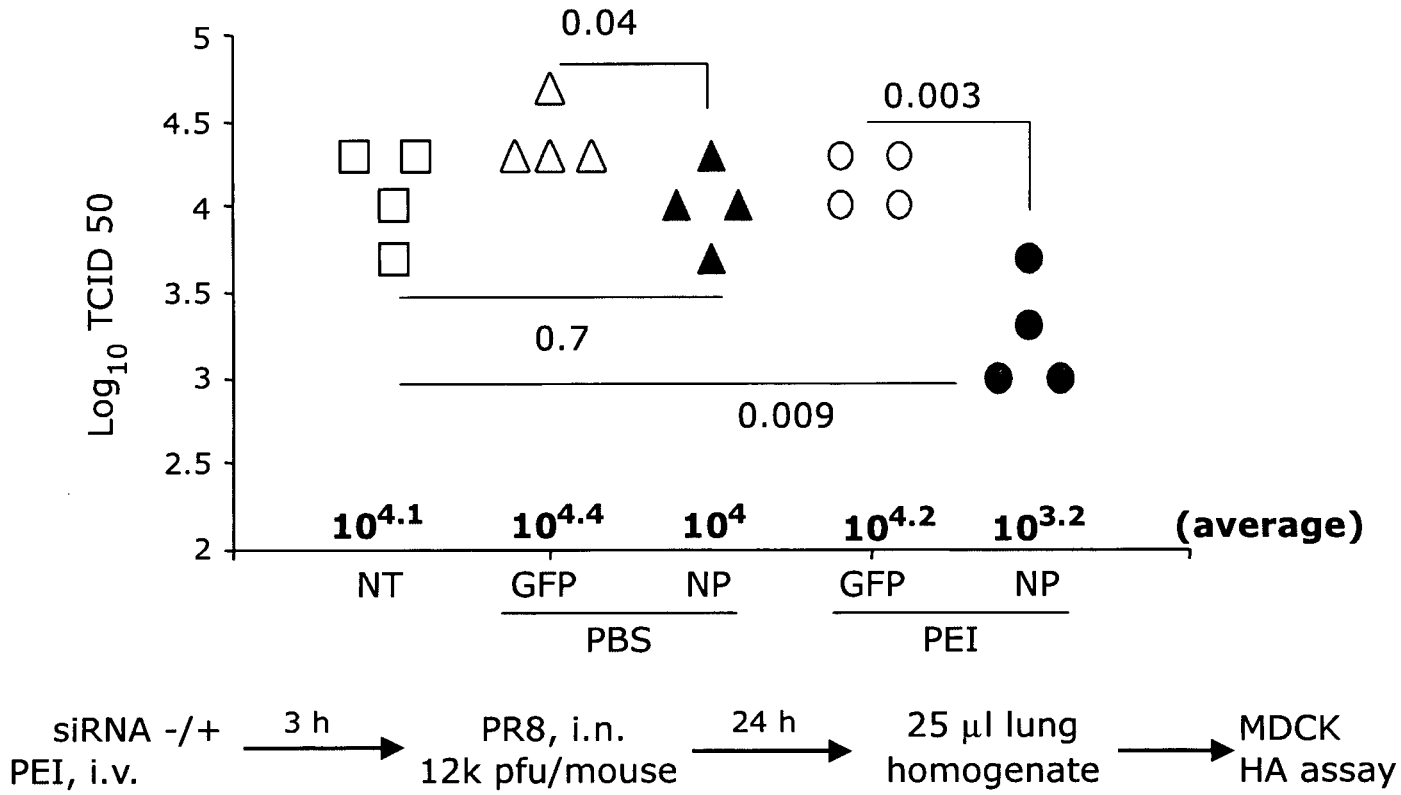


FIG. 22C

Additive/synergistic effect of siRNA against influenza virus in mice

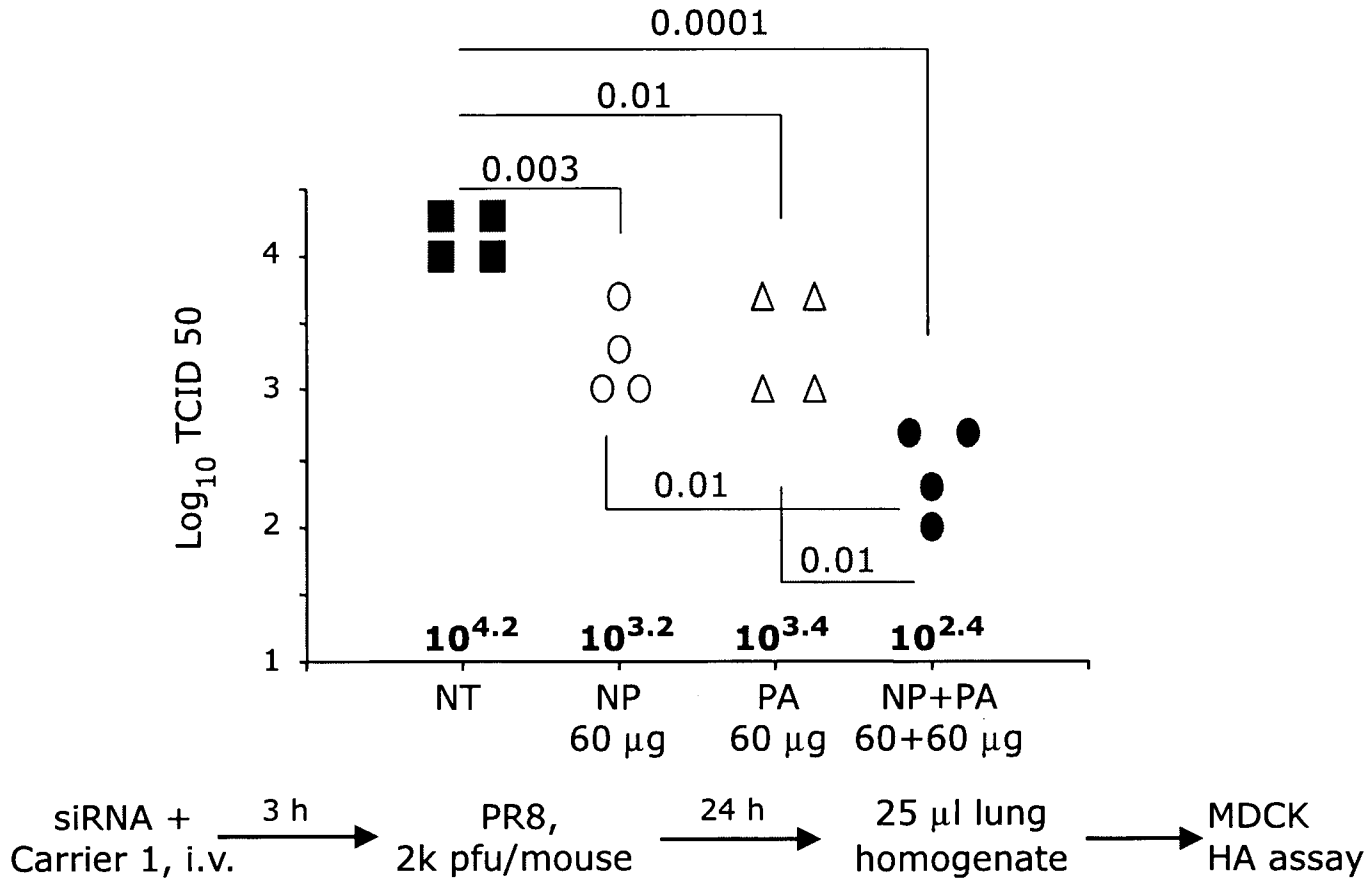


FIG. 23

siRNA inhibits influenza virus production in infected mice

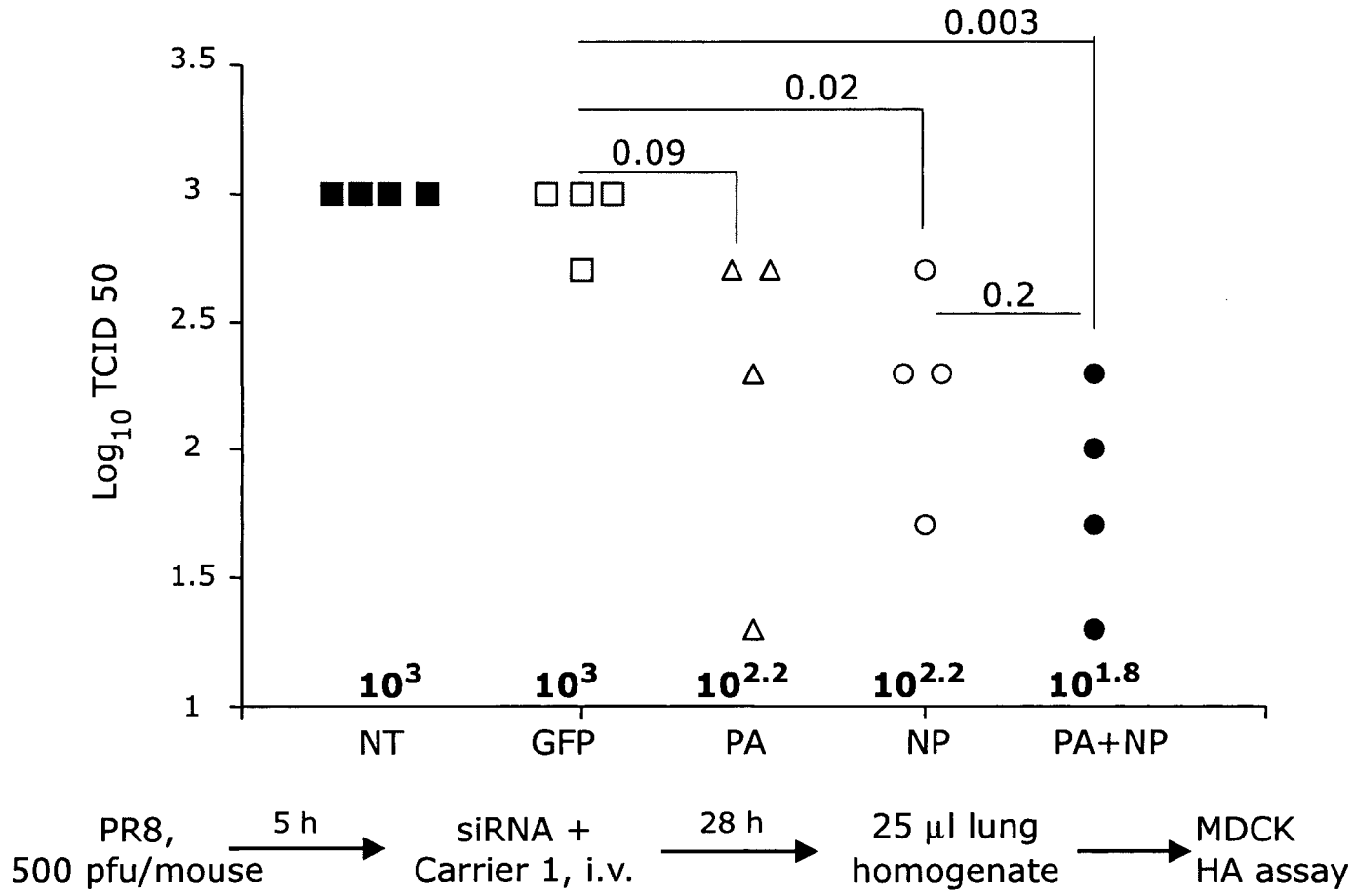
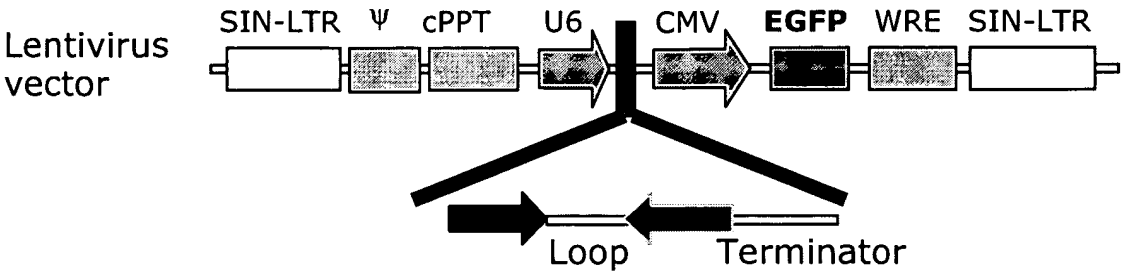


FIG. 24



NP-1496a shRNA

5'-GGAUCUUAUUUCUUCGGAGA UU C A A

UU CCUAGAAUAAAGAAGCCUCU AG A G

SEQ ID No: 271

FIG. 25A

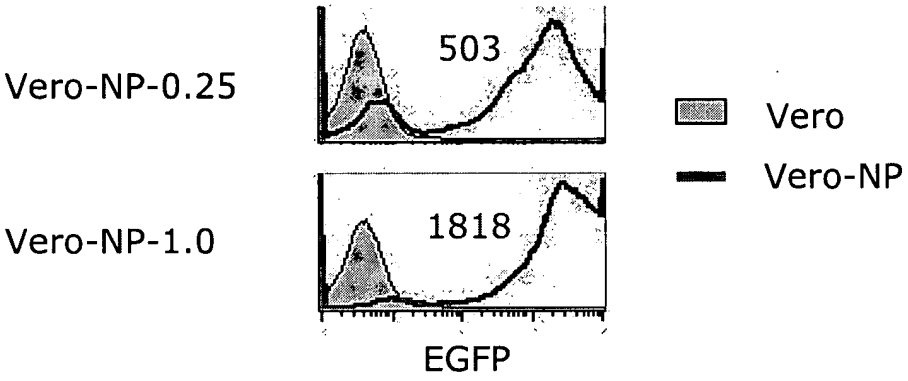


FIG. 25B

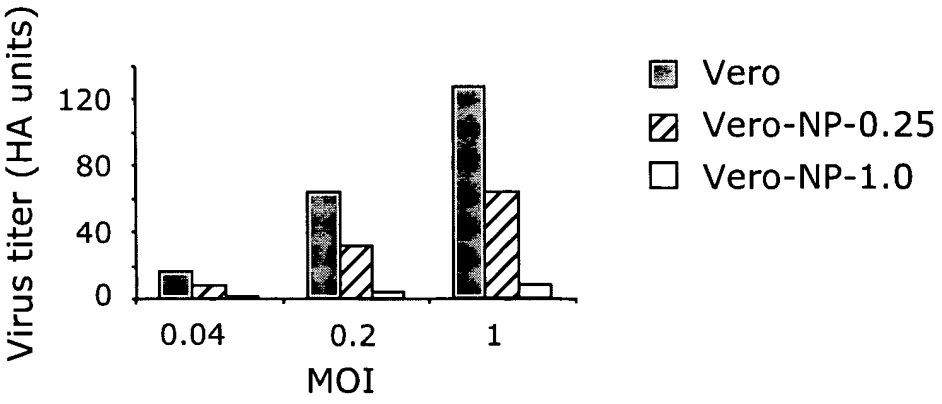


FIG. 25C

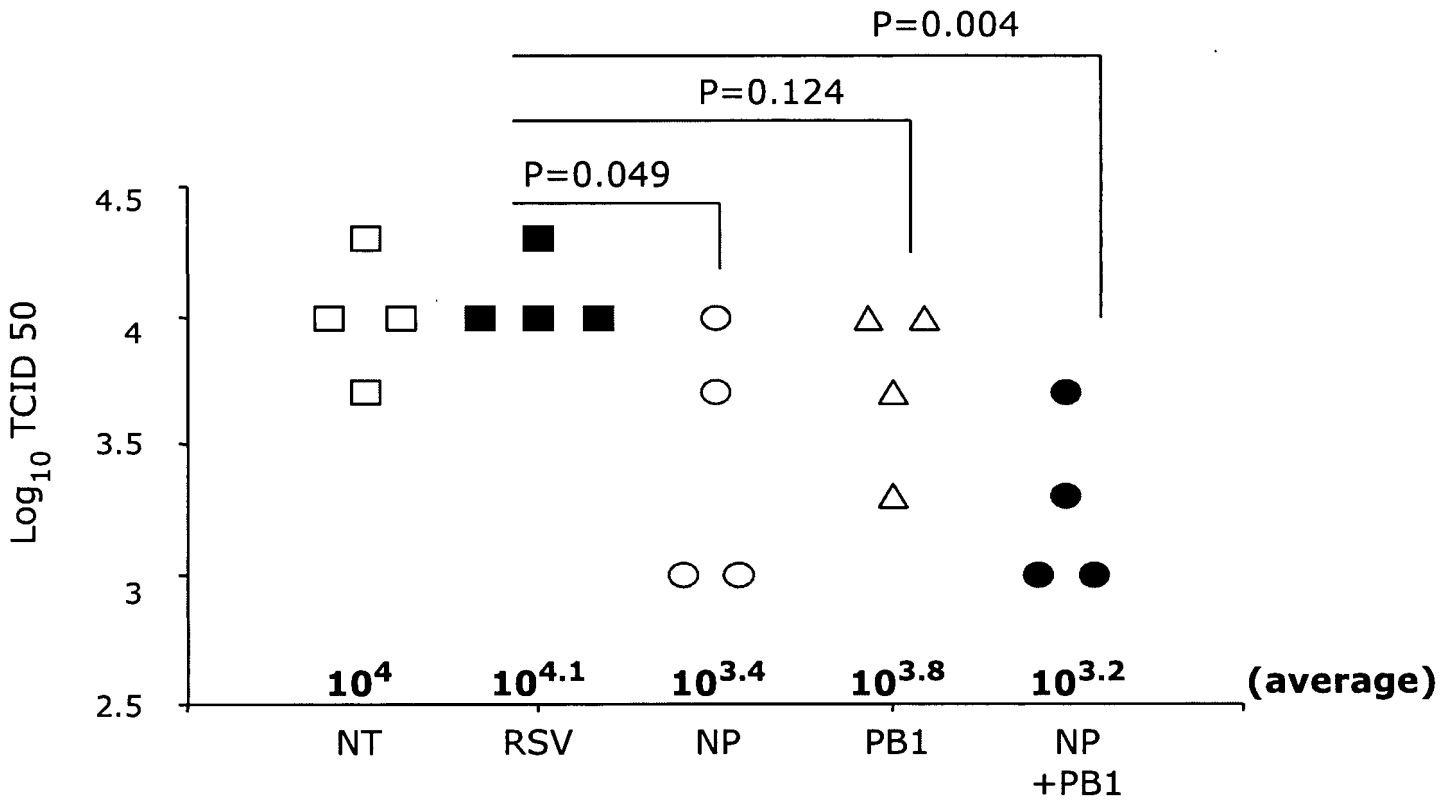

P=0.004
P=0.124
P=0.049
4.5
4
3.5
3
2.5
Log10 TCID 50
10^4
10^4.1
10^3.4
10^3.8
10^3.2
(average)
NT
RSV
NP
PB1
NP
+PB1

FIG. 26

Electrophoretic retardation of siRNA with poly-L-lysine

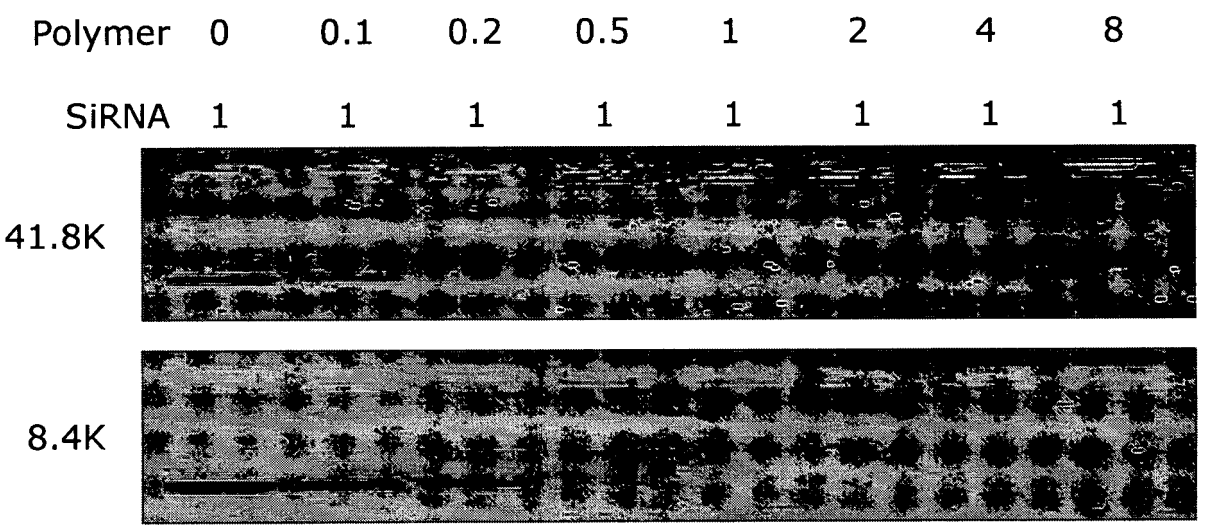


FIG. 27A

BEST AVAILABLE COPY

Electrophoretic retardation of siRNA with poly-L-arginine

PLA	0	0.02	0.06	0.17	0.5	1.5	4.5	13.5	43.5
SiRNA	1	1	1	1	1	1	1	1	1

FIG. 27B

BEST AVAILABLE COPY

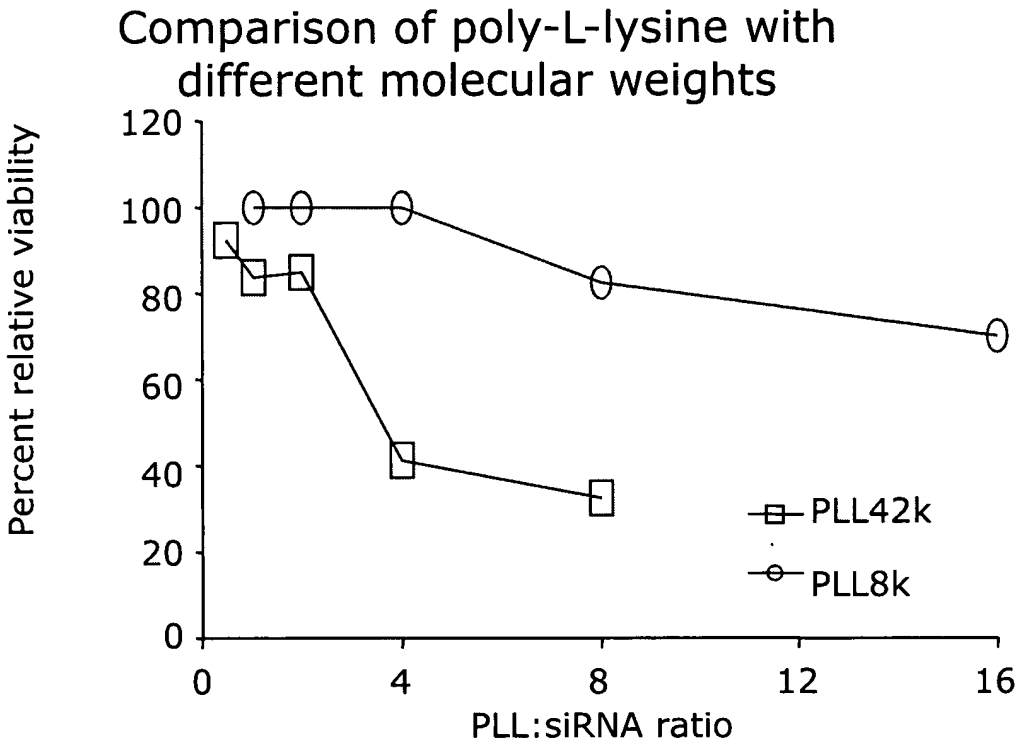


FIG. 28A

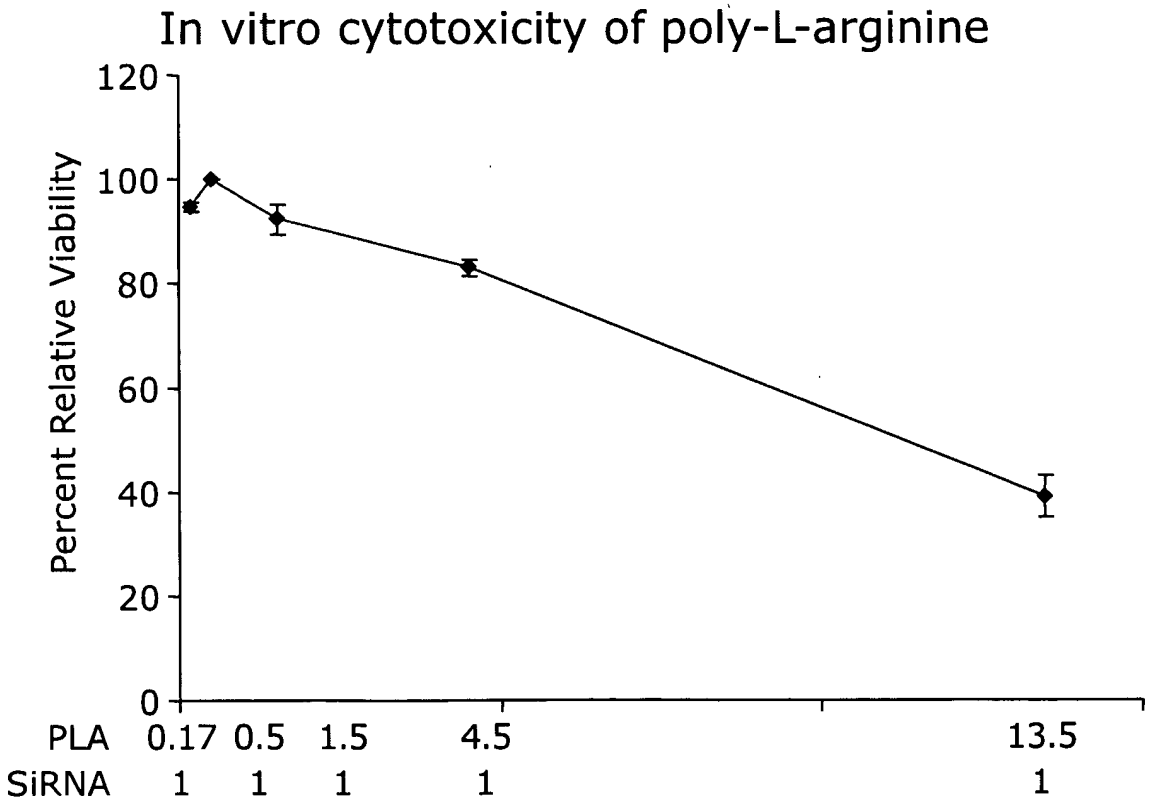
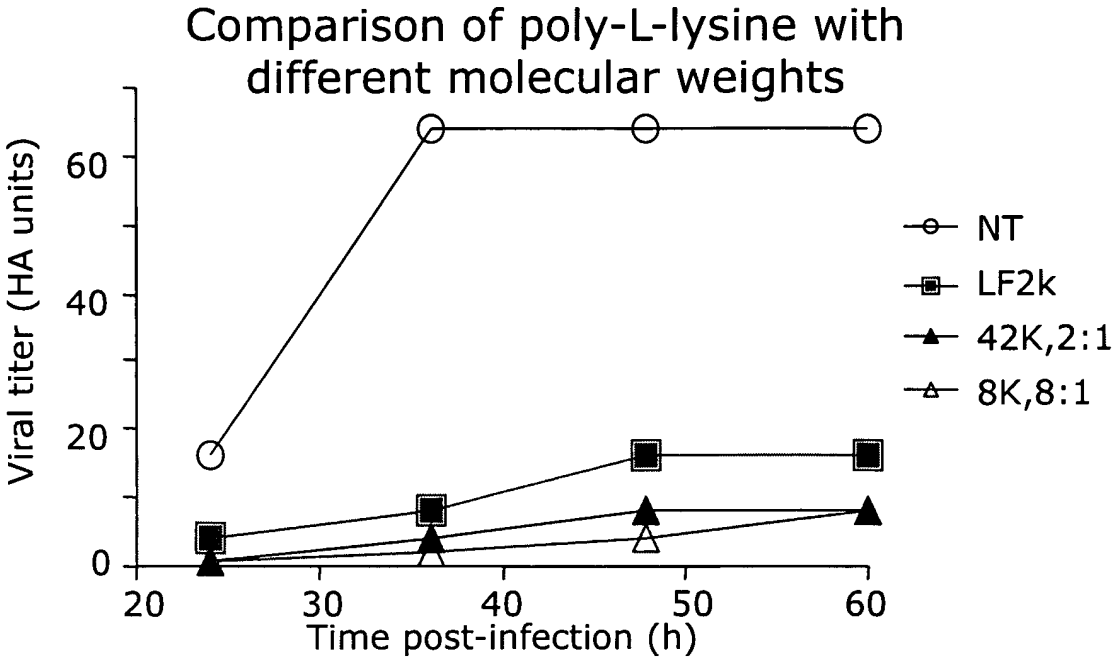


FIG. 28B



siRNA: $4x10^{-10}$ **M**
42K PLL: $2.9x10^{-10}$ **M**
8.4K PLL: $57x10^{-10}$ **M**

FIG. 29A

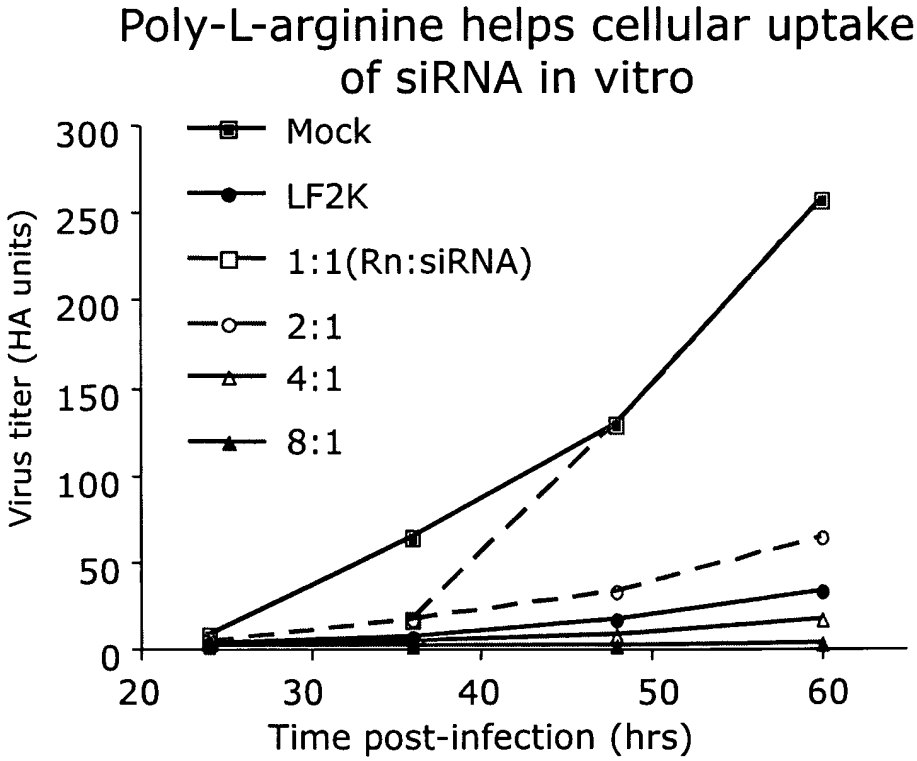


FIG. 29B